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DIPOLAR ASSOCIATION AND HYDRATION OF N-METHYL-
2-PYRROLIDONE IN SOME NON-HYDROXYLIC SOLVENTS

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DIPOLAR ASSOCIATION AND HYDRATION OF N-METHYL-
2-PYRROLIDONE IN SOME NON-HYDROXYLIC SOLVENTS

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DIPOLAR ASSOCIATION AND HYDRATION OF N-METHYL-2-PYRROLIDONE IN SOME NON-HYDROXYLIC SOLVENTS

CHAPTER I

INTRODUCTION

The Hydrogen Bonding of Lactams and Amides

A "hydrogen bond" is the term applied to describe the interaction between an acceptor group, A-H, acting as Lewis acid, and a donor atom or group B acting as a Lewis base. Acceptor groups are typically any labile hydrogen bound to an electronegative atom such as, nitrogen, oxygen, or halogen, although other functional groups are known, e.g. acetylenic hydrogens. Donor atoms are almost exclusively nitrogen and oxygen. Energetically, hydrogen bonds are much weaker than ionic and covalent bonds, normally falling in the range -3 to -10 kcal/mole per bond. However, an enthalpy change of this order of magnitude is not unique to hydrogen bonding phenomena. For example, the association of iodine with N, N-dimethylacetamide in carbon tetrachloride has a change of enthalpy of -5.1 kcal/mole. Generally, the working definition of a hydrogen bond proposed by G. C. Pimentel¹ has been found satisfactory: "A hydrogen bond exists between a functional group A-H and an

atom or group of atoms B in the same or different molecules when (a) there is evidence of bond formation and (b) when there is evidence that this new bond linking -A-H and B specifically involves the hydrogen atoms already bonded to A. "

While part a) may be satisfied in many ways, part b) is presently only satisfied by spectroscopic methods. Direct evidence for the participation of the hydrogen in the bond is obtained when a new A-H stretching band is observed at lower frequencies than the non-bonded vibration and the new band is broadened.

It is well established that primary and secondary amides and secondary lactams are both acceptors and donors in the hydrogen bonding sense. The self-association of amides has been extensively studied in a variety of solvents and by a variety of methods (see reference 1 for work prior to 1957 and references 2 and 3 for work up to the present). It is generally recognized that lactams, which exist in the cis- configuration (N-H hydrogen on the same side of the N-C bond as the carbonyl oxygen) form cyclic dimers while secondary amides (trans- configuration) form predominately chain polymers. Recently, Fruwert, Dombrowski and Geiseler⁴ have shown that the primary amides, acetamide, propanamide and butyramide apparently form only cyclic dimers up to 0.05 M in carbon tetrachloride and have an association enthalpy of -6.5 to -6.7 kcal/mole per hydrogen bond.

In the past few years there has been increasing interest in the

hetero-association of amides with various acceptor groups. Takahashi and Li⁵ investigated the association of the t-butylamine and aniline with N-methylacetamide and N,N-dimethylacetamide in chloroform solution by nuclear magnetic resonance spectroscopy. Taking into account the association of CHCl_3 with the donor molecules, it was found that aniline is a slightly better acceptor than t-butylamine and that N,N-dimethylacetamide is a better donor than N-methylacetamide. Apparently the authors did not consider the association between the N-H hydrogen of N-methylacetamide and the lone electron pair of nitrogen to be significant.

Earlier the same investigators had studied the association of 2-propanol with N-methyl- and N,N-dimethylacetamide in carbon tetrachloride. By adjusting the concentrations of the alcohol so that its self-association was negligible, a 1:1 association constant of $5.02 \text{ (mole/liter)}^{-1}$ at 24°C and a $\Delta H = -4.1 \text{ kcal/mole}$ were found with N-methylacetamide and $K = 2.56 \text{ (mole/liter)}^{-1}$ at 29°C and a $\Delta H = -2.4 \text{ kcal/mole}$ for the dimethyl derivative. In this case the N,N-dimethylacetamide appears to be a poorer donor toward alcohols than N-methylacetamide, just the opposite order found for amines.

This difference in donor properties of the same group toward different acceptors illustrates a very important point in hydrogen bonding studies: that is, if the hydrogen bonding properties (basicities) of various functional groups are to be meaningfully determined, they must

be allowed to interact with the same acceptor group (A-H). Recent research from this laboratory has involved the use of water, the prime example of a hydrogen bonding molecule, as the common A-H group. In connection with this study several sensitive colligative and spectroscopic techniques have been developed.^{7, 8}

After the initial decision had been made to study the hetero-association between water and amides, N-methyl-2-pyrrolidone (NMP), a lactam, was chosen for several reasons:

- 1) five-membered heterocyclic rings commonly occur in biologically important molecules, such as deoxyribonucleic acid (DNA), which contains both deoxyribose and purine bases, and proteins, such as beef oxytocin, which contains the 2-pyrrolidone residue in its peptide chain,
- 2) N-methyl-2-pyrrolidone is readily available commercially at moderate cost (\$11/kilogram),
- 3) it is reasonably easily purified,
- 4) it can be kept stable for long periods in the absence of oxygen,
- 5) N-methyl-2-pyrrolidone is quite soluble in the common organic solvents, and
- 6) since this compound does not contain an acidic hydrogen (N-H), self-association by hydrogen bonding would not complicate the equilibria in solution.

As implied in reason 1) the hydration of NMP was chosen as a

model for the hydration of a peptide bond. The importance of hydration in the study of the behavior and structure of proteins can hardly be over-emphasized. Due to the limited solubility of protein molecules in organic solvents, most studies of proteins involve the use of aqueous solutions. For example, the approximate size and shape of protein molecules in solution are frequently inferred from frictional coefficients obtained from diffusion or sedimentation experiments. But, the volume of the protein obtained in this manner always includes its hydration shell. Several attempts⁹ have been made to split the effective volume, V_e , found from any pair of hydrodynamic experiments into a volume of the protein and a volume of the water, such as $V_e = \frac{M\bar{v}}{N} + \frac{Mw}{N\rho_0}$ where $\frac{M\bar{v}}{N}$ is the volume of the dry protein and $\frac{Mw}{N\rho_0}$ is the volume of water bound to it. However, Scheraga¹⁰ points out that the volume of bound water obtained in this way does not have any physical significance, since it has been assumed that the partial specific volume of the protein in solution is its specific volume and that the density of the bound water is the same as that of the bulk solvent. Indeed, Scheraga concludes a lengthy diatribe on the subject with the statement; "Further, it is not possible to calculate hydration from hydrodynamic measurements, and no reality should be attached to w-values calculated in this manner."¹¹ Thus, if the hydration of proteins can not be inferred from hydrodynamic studies in aqueous solution, less direct methods must be employed.

Among the alternate methods possible for the study of the

hydration of proteins is a study of the absorption of water by the solid compound. A notable experiment conducted along these lines is that of Falk, Harteman and Lord,^{12, 13, 14} who determined the adsorption isotherm for the sodium and lithium salts of deoxyribonucleic acid (DNA) and water. It was found that the data could be fit up to 80% relative humidity by a simple B. E. T. equation, $A = BCX/(1-X+CX)(1-X)$, where A is the total water absorbed, B and C are arbitrary constants related to the quantity of water absorbed by the mono- and multi-layers, respectively, and X is the relative humidity (activity, p/p^0) of water. B was found to be about 2.0 molecules of water per nucleotide (a nucleotide is a subgroup of the DNA molecule composed of a base-sugar-phosphate complex) for both the salts, while C was 21 for the NaDNA and 36 for LiDNA. The negative deviation from this B. E. T. equation at activities greater than 0.8 was attributed to a swelling of the nucleotide polymer, which requires energy. Direct evidence for the swelling had been obtained by X-ray studies at the same approximate humidity.¹⁵ Later,¹⁴ infrared spectroscopic analysis of NaDNA films at varying humidities indicated that the first group to hydrate was the phosphate group, with possibly some contribution from the etheral oxygen of the deoxyribose ring. At approximately 65% relative humidity the hydration sphere of the phosphate group was complete at 5-6 water molecules per nucleotide. Above 75% relative humidity DNA undergoes a structural change to a more highly ordered form which was taken to be the form where the

base pairs are perpendicular to the axis of the helix as had been established by X-ray work.¹⁶

Falk has recently extended his hydration studies to include the nucleotides; Ribonucleic acid (RNA)¹⁰⁰, soluble RNA, polyriboadenylic acid and nucleohistone¹⁰¹. All four systems show nearly an identical behavior as DNA, a fact which lead the author to conclude that the hydration of nucleotides is largely controlled by the phosphate groups and is not strongly affected by the cation or the nature of the secondary structure. Interestingly, above 75% relative humidity the data were better described by the Harkins-Jura equation, which assumes a liquid-like adsorbed phase.

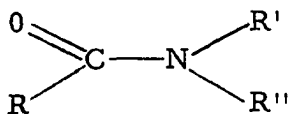
Another indirect method giving insight into the hydration of proteins in aqueous solution is the study of association reactions in non-aqueous solvents. This method is generally limited, however, to model peptide groups due to the low solubility of proteins in these solvents. Prior to this work, to my knowledge, only three quantitative hydration studies have been reported; the first by Worley², second by Grigsby³ and the other an NMR investigation of N,N-dimethylacetamide in cyclohexane by Takahashi and Li.¹⁷ Worley measured the extent of hydration by following the absorbance of the antisymmetric stretching frequency of the free O-H of the bound water as a function of water activity and lactam concentration. Only 1:1 complexes were found for N-methyl-2-pyrrolidone up to a concentration of 0.04 moles/liter and water activities

of approximately 0.95. In the NMR work by Takahashi and Li it was necessary to use amide mole fractions of 0.5 to 0.99 with water concentrations of 0.003 to 0.002 m.f. in order to see a resonance due to the bound water. In these concentration regions 1:1 and 1:2 water to amide complexes were proposed. However, by their method, the equilibrium constant for the 1:1 constant could not be evaluated. The 1:2 complex was found to have a stepwise constant of 0.24 mole l^{-1} at 35°C and a ΔH of -3.6 kcal/mole .

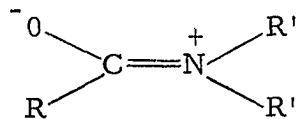
To the author's knowledge, the work described in the following chapters represents the only non-spectroscopic quantitative investigation of the hydration of a lactam molecule as model peptide compound. However, before the hydration of NMP can be discussed properly some background into the structure and relative basicities of the two sites in amides and lactams is needed. These topics are treated in parts II and III of this introduction.

The Structure of the Amide Group

The structure of the amide group is probably best described in terms of the resonance forms illustrated below. These principal forms, however, do not contribute equally, since A would be expected to predominate over B.



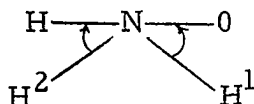
A



B

The fact that there is indeed a delocalization of π -electron density between the lone pair electrons of the nitrogen and oxygen would appear to be well established from the extensive work that has accumulated on amide structures.

The first requirement for resonance to exist in a structure is that it must be planar. X-ray crystallographic,¹⁸ microwave,^{19, 20} infrared²¹ and nuclear magnetic resonance²² (NMR) spectroscopy data all demonstrates that the six atoms involved in the amide group are coplanar or nearly coplanar; with but one notable exception. C. C. Costain and J. M. Dowling²³ have shown by a careful microwave spectroscopic study of formamide along with its deuterated and N¹⁵ isotope derivatives that a shallow pyramid better describes their data. They find dihedral angles for H¹N-CO of 7° 12' and for H²N-CH of 12° 52'.

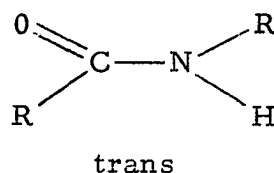
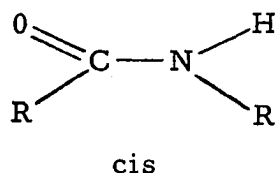


In addition, Costain and Dowling found it necessary to postulate an "inversion" of the hydrogens H¹ and H² in order to explain the intense and strongly anharmonic satellite bands which accompany the main rotational absorbances.

The second requirement for validity of the resonance is that there should be considerable double bond character associated with the amide C-N bond.

Pauling²⁸ originally estimated that there should be a barrier to internal rotation of approximately 30 kcal/mole. However, probably the first experimental evidence for such a barrier in amides was obtained by Phillips,²⁹ who observed two resonance bands for the methyl groups of N,N-dimethylformamide which were proportional to the applied field. The latter observation shows that the bands are not split by coupling with the formyl proton. Therefore, this difference in chemical shifts for the N-methyl protons implies a stable configuration^a in which the rate of reorientation is much less than the resonance frequency or, that $\tau_A \gg \frac{\sqrt{2}}{2\pi} (\nu_A - \nu_B)$ where τ_A is the mean lifetime in state A (one configuration) and where ν_A and ν_B are the resonance frequencies for state A and B.

However, the apparent anomaly noted previously in the case of formamide is supported in that it is the only amide for which there is evidence of a cis-trans equilibrium at ambient temperatures. Recently, La Plance and Rodgers,²⁴ following the earlier infrared spectral evidence,^{21, 25, 26} have shown by an NMR study of thirteen N-mono-substituted



^a Since the R group is in a different electronic environment in the two configurations, the proton resonance and coupling for the cis- and trans-forms will differ slightly, provided the reorientation rate is slower than the resonance frequency.

amides that all except the formamides exist in the trans configuration. By a careful assignment of resonance frequencies based largely on earlier work, it was concluded that the high field N-alkyl proton band was due to the cis configuration. Using these assignments and coupling constants they found 8% of the cis- configuration in pure N-methylformamide and 18% in N-t-butylformamide dissolved in benzene. In the case of amides all of this would seem to be adequately explained by a large potential barrier to internal rotation about the C-N bond.

Later, Gutowsky and Holm,³⁰ assuming a first order reorientation rate process, derived an expression relating k , the rate constant for reorientation, to $\Delta\omega$, the separation of the resonances for states A and B. Although it was necessary to solve this expression numerically, it was still possible to obtain a good estimate of the rotational energy barrier from the temperature dependence of $\Delta\omega$. This treatment yielded 7 ± 3 and 12 ± 2 for the respective potential barriers to internal rotation of N,N-dimethylformamide and N,N-dimethylacetamide.

Recently, Whittaker and Siegel,⁶¹ following up the initial work by Moriarty,⁶² have concluded from a thorough study of the effects of temperature, concentration and solvent on $\Delta\omega$, the separation of the N-methyl doublet in N,N-dimethylformamide, that the earlier values of E_a , the potential barrier to internal rotation, were too low. The reason proposed for this discrepancy was that an erroneous value of $\Delta\omega_\infty$, the separation at sufficiently low temperatures to "freeze-out" internal rotation, had been used previously. Whittaker and Siegel found $\Delta\omega$

continued to rise at a steady rate with a decrease in temperature even to the limit of their probe (-55°). Furthermore, $\Delta\omega_{\infty}$ was found to be solvent and concentration dependent. However, the formyl and mean N-methyl proton resonances were temperature and concentration independent. The former observation rules out hydrogen bonding at the formyl proton. Since the N-methyl doublet was affected symmetrically, it was hypothesized that the change in $\Delta\omega$ with concentration, temperature and solvent was due to dipolar association. The authors claim that the magnetic anisotropy (related to the induced dipole) produced in the carbonyl bond would affect the N-methyl doublet symmetrically. Thus, it was concluded that only the higher temperature values of $\Delta\omega$, where dipolar association is negligible, should be used for evaluation of E_a . It was necessary, however, to fit $\Delta\omega_{\infty}$ as a parameter to obtain a straight line relationship between $1/\tau$ and $1/T$. Proceeding in this manner, the values of the internal barrier given in Table I were obtained.

TABLE I
 E_a VALUES FOR N,N-DIMETHYLFORMAMIDE (DMF)
IN SEVERAL SOLVENTS

m. f. of DMF	solvent	$\Delta\omega_{\infty}$ c. p. s.	E_a kcal/mole
1.000	pure	8.70	15.9 ± 2.0
0.0858	acetone-d	8.25	16.8 ± 2.0
0.105	CFCl_3	6.45	11.3 ± 2.0
0.0633	*HMDS	2.88	9.4 ± 1.0

* hexamethyldisiloxane

Raman spectroscopy has also contributed information concerning hindered rotation in amides. Based on an approximate out-of-plane normal coordinate analysis at low frequencies, Miyazawa¹⁴ was able to estimate a barrier height of 14 kcal/mole by assigning the weak bands at 206 cm^{-1} and 356 cm^{-1} to the C-N torsional mode for N-methylacetamide and N-methylformamide.

Despite the approximate nature of these determinations, one can see from the magnitude of E_a that considerable double bond character is associated with the C-N bond as demanded by the resonance concept.

Additionally, this double bond character should be reflected in a shortened C-N bond and a lengthened C=O bond compared to that of, say, an amine and a ketone. Pimentel¹⁸ lists the following average values, derived from a large number of compounds, for these bond lengths:

Bond	C-N	C=O
Normal Single	1.48	1.42
Peptide	1.32	1.24
Normal Double	1.24	1.20

Utilizing Pauling's method of calculation and these data, Vaughan and Donohue¹⁵ calculate a 30-40 percent double bond character for the C-N bond and a 70-60 percent double bond character for C=O in a peptide.

More recently, Morris and Orville-Thomas³³ has recalculated the bond orders for several primary amides by assuming the wave function to be; $\Phi = \Phi_s + \lambda \Phi_p$ where λ is a mixing coefficient for the s and p orbitals involved.

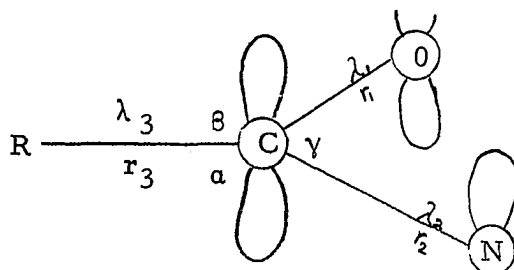
Following Coulson³⁴ and assuming the nitrogen to be sp^2 hybridized, it was possible to estimate the percent s- and p- character for the three bonds about the carbonyl carbon atom from the following relationships;

$$\lambda_1 = [-\cos \alpha / \cos \beta \cos \gamma]^{1/2}$$

$$\lambda_2 = [-\cos \beta / \cos \alpha \cos \gamma]^{1/2}$$

$$\lambda_3 = [-\cos \gamma / \cos \alpha \cos \beta]^{1/2}$$

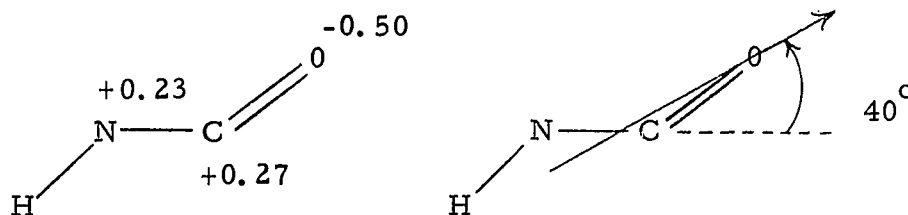
$$\% s = 100[1/1 + \lambda^2] \text{ and } \% p = 100[\lambda^2/1 + \lambda^2],$$



Application of this method to several typical amides yields 41 to 51% s-character for C=O and 21 to 33% s-character for C-N. On this basis Orville-Thomas concludes that it is wrong to consider the oxygen to be sp^2 hybridized. In other words, in an amide group we have an electronic situation which is not well described by the valence bond approach.

Additional evidence supporting the resonance concept as applied to amides is derived from dipole moment studies. In 1955 Kotera, et al.,³⁵ found that dipole moments of the series $C_6H_5(CH_2)_mNHCO(CH_2)_nC_6H_5$ ranged from 3.9 to 3.6 D and generally increased with increasing m and decreasing n. The smaller moments found for the anilides (m=0) was

explained by a decreased nitrogen-carbonyl oxygen resonance contribution resulting from the three possible nitrogen-phenyl resonance forms. Based on bond dipoles the authors concluded that the preferred configuration was trans and that the usual amide resonance form contributed approximately 0.6 D units to the observed dipole moments. Then, from an LCAO M.O. treatment using data for N-methylacetamide (1.21 and 1.36 Å for C=O and C-N) and assuming an interior N-C-O angle of 120° , they calculated the following distribution of charges:



Significantly, the dipole lies nearly in the same direction as the C=O bond.

Along the same line, Lee and Kumler³⁶ have shown that N-alkyl substitution increases the dipole moment of lactams and amides. For example, 2-piperidone (six-membered ring) has a dipole moment of 3.83 D, N-methyl-2-piperidone, 4.01 D; 2 pyrrolidone, 3.79 D; and N-methyl-2-pyrrolidone, 4.06 D.^b These results were interpreted in terms of the electron donating properties of the methyl groups, which allow the nitrogen to take a greater positive charge, thus increasing the contribution of the ionic resonance form. In other words, these results

^bFischer³⁷ obtained a value of 4.09 D for this compound.

imply that the bond moment of N-H is greater than that of N-C. It is interesting that if the three nitrogen bond angles are nearly equal, the N-C bond moments will essentially cancel leaving the resultant dipole virtually coaxial with the C=O bond.

Recently, the effect of bulky alkyl substitution on the dipole moments of several amides has been investigated by Thompson and La Planche.³⁸ Even for N-butyl-N-methylpivalamide (a trimethylacetamide), which cannot be planar assuming the nonbonding radius of a methyl group to be 2 Å, a dipole moment of 3.57 D was found. Therefore, it was concluded that either the usual ionic resonance form does not contribute nearly as much as previously thought, or that the potential barrier to rotation about the C-N bond is symmetrical with two or more maxima.^c

In summary, it must be concluded that the resonance concept is generally satisfactory in explaining and predicting the structural and electronic properties of the amide group. However, one aspect of the structure of mono-substituted amides remains to be adequately explained (indeed, it never even seems to be discussed); that is, why is the trans configuration preferred almost to the exclusion of the cis? The usual argument of steric hindrance appears to break down for the formamides, which also show a strong preference for the trans form.

^cIt has been shown³⁹ that if there are two or more symmetric barriers to internal rotation the effect on the electric moment will be the same as for free rotation.

The Basicity of the Amide Group

Now that the structure of the amide group has been reviewed a discussion of the basicity of amides will be more intelligible. Most of the following will relate to information gleaned from protonation studies, since little information on relative basicities of various amides has been obtained, as yet, from hydrogen bonding studies. Furthermore, it will be assumed, ad hoc, that protonation and hydrogen bonding are simply different manifestations of the same phenomenon. This is perhaps reasonable since protonation is thought to begin with the formation of a hydrogen bond. In addition, no amide basicities based on the Hammett scale are included, for amides have been shown not to follow this relationship.^{40, 41}

One of the earlier thorough works on the relative basicities of amides was that of Huisgen and Brade.⁴² In this study pK_a values were determined for a series of amides in which the N- and C- substituents were varied systematically. Potentiometric titrations of the amides dissolved in glacial acetic acid with perchloric acid were followed by a chloranil and tetrachlorohydroquinone electrode system as proposed by Hall and Conant.^{43, 44} The resulting conjugate acid dissociation pK_a^d values taken at half-neutralization were converted to a "water scale"

^dBernard O. Heston and Norris F. Hall, J. Am. Chem. Soc., **55**, 4729 (1933), however, have shown that due to solvation the proper E^o for the chloranil electrode in glacial acetic is ± 0.680 v instead of $E^o = + 0.664$ v proposed by Hall and Conant.

by the relationship;

$$\text{pK}_a (\text{water}) = \text{pK}_a (\text{acetic acid}) + 1.70$$

The results are shown in Table II.

TABLE II
pK_a VALUES FOR VARIOUSLY SUBSTITUTED AMIDES

Compound	pK _a
formamide	-0.48
N-methylformamide	-0.04
N-dimethylformamide	-0.01
N-n-butylformamide	0.03
N-benzylformamide	-0.33
acetamide	0.11
N-methylacetamide	0.80
N-ethylacetamide	0.79
N-n-butylacetamide	0.84
N-cyclohexylacetamide	0.77
N-benzylacetamide	0.31
N-benzyltrimethylacetamide	-0.43
N-methylbutyramide	0.79
N-benzhydrylformamide	-0.63

The authors argue that, since N-substitution has less effect on the basicity of amides than for a corresponding series of amines, the site of protonation must be further removed from the electronic effect; that is, protonation occurs at the oxygen. However, in the light of the present structural knowledge of amides, it is perhaps more significant that the formamides show the least basicity. It was shown in Part II that formamide is the only amide thus far studied that has been found to be non-planar and to possess a cis-trans equilibrium at room temperatures.

These structural anomalies imply that there is less contribution from the ionic resonance form in formamides, which would be reflected by lower basicities if O-protonation occurred.

Further evidence for the unusual properties of formamide relative to the other amides is afforded by other basicity measurements. Using the technique of Streuli,²⁷ whereby nitromethane-amide solutions are potentiometrically titrated with nitromethane-perchloric acid solution, Adelman⁶⁴ found conjugate acid dissociation constants for twenty N,N-disubstituted amides. Included were 5.02 and 3.17 for N,N-dimethyl and N,N-diethylformamide, while N,N-dimethyl and N,N-diethylacetamide had acid dissociation constants of 0.80 and 0.63, respectively. Interestingly, the order of these basicities ($K_b = 1/K_a$) would seem to be most compatible with O-protonation. Since formamide is the least nearly planar of the amides, less contribution to its structure would be expected from the ionic form; therefore the compound should be less basic. However, provided one accepts the resonance concept, N-protonation would seem to require formamide to be the most basic.

In another article by Huisgen, et al.,⁴⁵ the basicities of a series of lactams with five- to nineteen-membered rings were studied. In addition to the potentiometric method already described, a spectroscopic indicator technique⁴⁶ using 4-chloro-2-nitroaniline in the same solvent-titrant system was employed. The results are given in Table III. It is interesting to note that the five- and six-membered rings form the lower

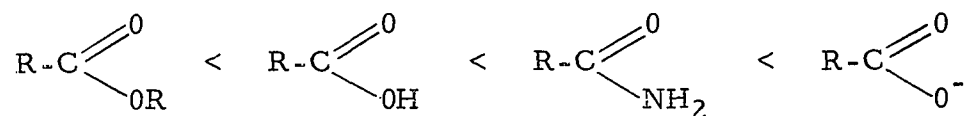
and upper limits of the basicity of lactams. The shift from generally decreasing basicities between the seven- and eight-membered rings to increasing basicities for the larger rings is attributed to a change from a cis to a trans configuration at these ring sizes (infra-red and ultra-violet spectral, as well as solubility data were offered as further evidence for this transformation). Since this series of lactams failed to show a sharp minimum in a plot of pK_a vs. ringsize as the corresponding polymethylenimines (aliphatic cyclic amines) do, it was further concluded that exocyclic protonation had occurred.

TABLE III

pK_a VALUES FOR A SERIES OF ALIPHATIC LACTAMS AT 25°C

Ringsize	5	6	7	8	9	10
Potentiometric method	-0.03	0.75	0.36	0.52	0.55	0.65
Indicator method	-0.33	0.64	0.27	0.42	0.37	0.58
Ringsize	11	13	14	16	19	
Potentiometric method	0.72	0.65	0.57	0.58	0.57	
Indicator method	0.57	0.52	0.46	0.52	0.47	

In general, for weakly basic compounds the following series is recognized:



The carboxylic acids have pK_a values of approximately -7, amides -1 to +1 and the carbonate anion around +5.

Most of the evidence for N-protonation of amides has been derived from vibration spectra. Usually the arguments derived from this method have been based on observation of shifts to lower frequencies of the N-H and C=O vibrations^e owing to protonation at the respective sites. 47, 48, 49

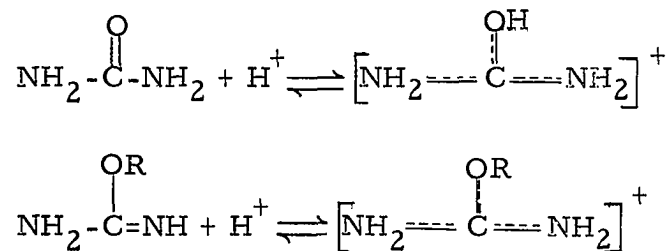
Typical of this type of study is that of M. Davies and L. Hopkins,⁴⁷ in which the spectrum of urea nitrate was examined. Since this analysis showed the typical N-H stretching frequency, $[\nu(\text{N-H})]$, doublet at a mean frequency of 3396 cm^{-1} (cf. a mean $\nu(\text{N-H})$ of 3230 cm^{-1} for urea) and in addition a doublet at a mean frequency of 3230 cm^{-1} (cf. to ammonium salts at 3200 cm^{-1}), and since no band typical of $\nu(\text{O-H})$ was found, it was concluded that N-protonation occurred in urea. In order to explain the observed monobasicity of urea, the authors estimated the resonance energy in urea to be approximately 10 kcal/mole, and a loss of 3 kcal/mole of this energy upon the formation of the mono-salt. Thus, the loss of the remaining 7 kcal/mole of resonance energy upon the formation of the di-salt combined with the electrostatic repulsion of the two closely spaced positive charges, would render the equilibrium constant for the addition of a proton to the second site experimentally

^eFor a thorough review of this aspect up to 1961 see A. R. Katritzky and R. A. Y. Jones, Chem. and Ind., 722 (1961).

undetectable. Furthermore, two bands in the carbonyl stretching frequency region were found for urea nitrate (1305 and 1675 cm^{-1}) at higher frequencies than the $\nu(\text{C=O})$ band for pure urea (1610 cm^{-1}) as would be expected from N-protonation.

More recently, however, Stewart and Muenster⁴⁸ have investigated the infrared spectra of dicyclohexylurea, dicyclohexylurea p-toluenesulphonate and their O^{18} isotopes. By comparison with spectra for known ionic and covalent compounds of urea the authors were able to show that the p-toluenesulphonate compounds were probably ionic. An isotopic shift of 17 cm^{-1} to lower frequencies was found for the carbonyl stretching frequency of the molecular compounds, which compared favorably with the same shifts in benzophenone and benzamide (29 and 24 cm^{-1} , respectively).⁴⁹ Although two bands were found in the carbonyl stretching frequency region for the p-toluenesulphonate salts, as Davies and Hopkins had for urea nitrate, these absorbances did not show an isotopic shift. However, the two bands at 1437 and 1135 cm^{-1} which were assigned to O-H bending and C-OH stretching, respectively, did show isotopic shifts of 10 and 6 cm^{-1} . In agreement with urea nitrate the spectra did not show an O-H stretching absorbance, but the authors proposed that either the absorbance was too weak, or that it was masked by the broad bands in the 2400 and 2600 cm^{-1} region. The authors offered further evidence for O-protonation in that, since O-alkyl ureas are about 10^{10} times as basic as urea, the difference must be attributed to resonance energies

of the neutral molecules because the resonance energies of the ions would be about the same.



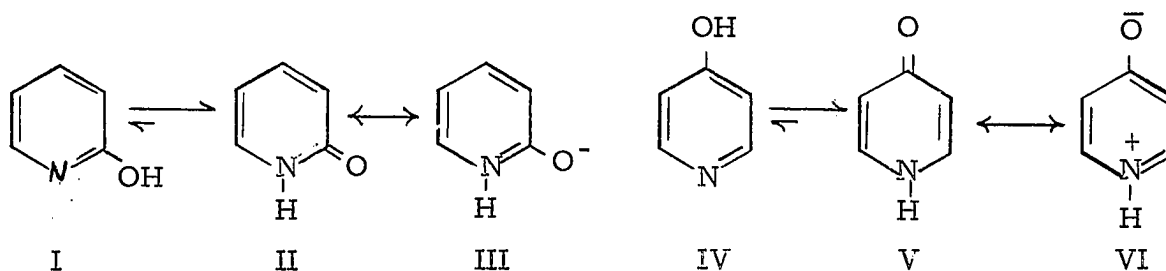
In further infrared work with amides, Denys Cook⁶³ was able to assign by isotopic shifts the bands near 1250 cm^{-1} in solid amide and lactam salts to an O-H deformation mode. Some of his results for these compounds are shown in Table IV.

TABLE IV
DEFORMATION MODES AND ISOTOPIC SHIFTS
IN cm^{-1} FOR SOME SOLID AMIDE SALTS

Compound	δOH	$\Delta\delta\text{OH}$ (avg. if split)	δOD	$\Delta\delta\text{OD}$	$\delta\text{OH}/\delta\text{OD}$
N, N-dicyclohexylacetamide	1282	0	1086	0	1.18
N, N-dimethylacetamide	1253	147	1003	90	1.25
N, methyl-2-pyrrolidone	1265	74	972	60	1.30

The chief spokesman for the N-protonation school has been E. Spinner of the National University of Australia who bases most of his argument on the rejection of the concept of π -electron delocalization in

conjugated systems. In connection with his work on aromatic heterocyclic compounds,⁵² among which were 2- and 4-hydroxypyridines, it was shown by the absence of a strong Raman absorbance at approximately 1000 cm^{-1} (characteristic of a fully aromatic six-membered ring) that these compounds exist predominantly in the amide form; that is, II



Furthermore, in the next article of the series,⁵³ it was shown that the same absorption was missing for the 2- and 4-oxypyridines in strong aqueous acid solution (up to 1 solute: 6HCl). Strong absorbance bands above 1700 cm^{-1} in the infrared spectra of these compounds were taken as evidence for the presence of a carbonyl oxygen. Since the O-protonated form of these compounds should be fully aromatic as indicated above, it was concluded that predominantly N-protonation occurred in 2- and 4-oxypyridines.

Information concerning the basicities of amides has been derived also from spectral studies of the coordination of amides with metal cations and molecular compounds, such as boron trichloride. However, studies with solids are not considered completely applicable to solution behavior, since in the solid, geometry may become important than small differences in basicity of the coordination site. Along these lines an

interesting infrared study of the interaction of iodine with several N-disubstituted amides in carbon tetrachloride has been conducted by Schmulback and Drago.⁵⁸ Based on the observations that in the presence of iodine the carbonyl stretching frequency shifts by 43 cm^{-1} to lower fields and that the C-N stretching frequency at 1460 cm^{-1} increases to 1530 cm^{-1} , it was concluded that predominantly O-iodination occurred in amides. By comparison with ketones such as acetone and cyclopentanone it was found that the $\text{N}(\text{CH}_3)_2$ group was approximately ten times as effective in increasing the basicity of the carbonyl oxygen toward iodine as was the methyl group.

Nuclear magnetic resonance studies have provided significant information regarding the site of protonation in amides. In what appears to be a thorough study, Berger, Lowenstein and Meiboon⁵⁴ (and at nearly the same time Fraenkel and Niemann⁵⁵) have analyzed the NMR spectrum of N-methylacetamide as a function of concentration and acidity and have concluded that predominantly O-protonation occurs. Sketchily, their analysis proceeded as follows. The spectra of N-methylacetamide (NMA) shows a doublet for the N-CH_3 protons due to spin-spin coupling with the N-H proton. From the sharpness of this doublet at pH 5 it was concluded that the rate of exchange of the amide hydrogen had a half-time of greater than one second. The broad and indiscernible N-H resonance was thought to be a triplet arising from spin-spin interaction with the N^{14} nucleus along with a superposed quartet from the N-CH_3

protons. At lower pH the N-methyl doublet coalesced to a singlet, which was taken to mean that the N-H proton was exchanging so rapidly at these acidities that its spin-spin coupling was below detection. Importantly, however, this doublet was found to reappear at very high acidity, and at all acidities when diluted with dioxane, where the exchange was slowed sufficiently to allow spin-spin interactions. Complications occurred when it was found that under high resolution and at moderate acidities and basicities the N-methyl and C-methyl proton resonances were really a quadruplet. This contribution to the N-methyl resonance was removed by assuming a Lorentian envelope for the quadruplet. Exchange rates were determined from the broadening of both the N-methyl and water resonances as a function of acidity after being corrected for viscosity effects. The fact that both methods gave the same rate within experimental error indicated that virtually all the exchange occurred between water and the solute. Assuming a first order rate process, the specific rate, R , is given by;

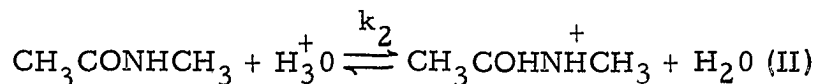
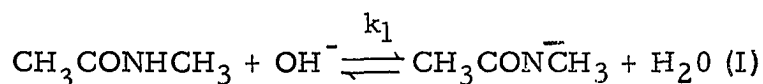
$$R \equiv 1/\tau = \frac{1}{[\text{amide}]} \cdot \frac{d[\text{amide}]}{dt}$$

where τ is the mean life-time between proton exchanges. It was found that R was independent of the amide concentration, but directly proportional to either the hydrogen or hydroxyl ion concentration as the case may be.

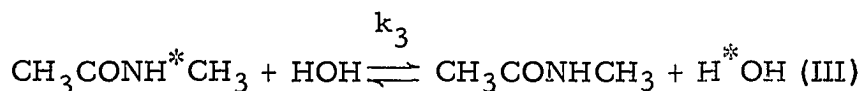
Proceeding in this manner, rate constants of $k_1 = (5.2 \pm 1.0) \times$

$10^6 \text{ M}^{-1} \text{ sec}^{-1}$ for $\text{pH} > 7$ and $k_2 = (3.8 \pm 0.4) \times 10^2 \text{ M}^{-1} \text{ sec}^{-1}$ for $\text{pH} < 7$

were determined for the equilibria:

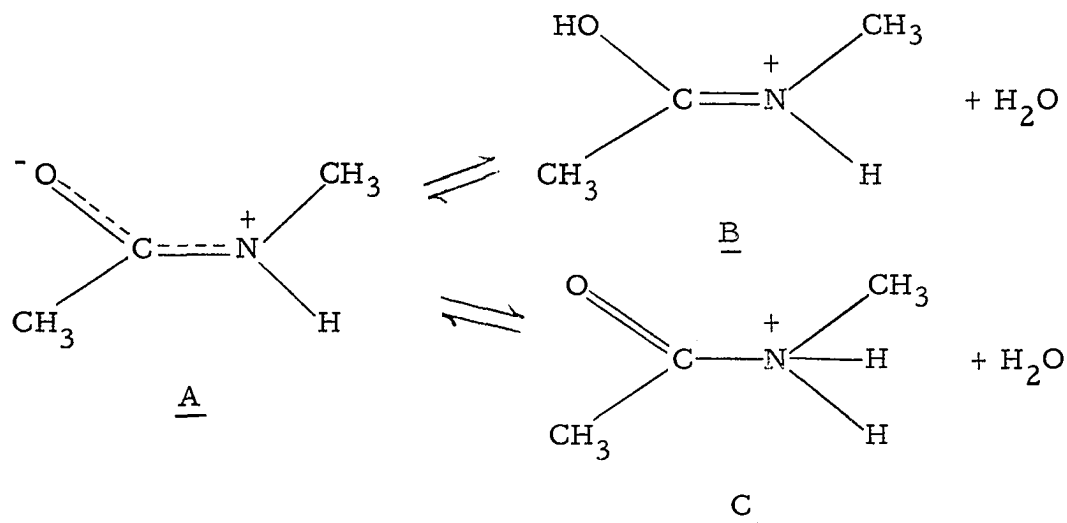


A third possible reaction



was estimated to have a $k_3 < 2 \times 10^{-3} \text{ M}^{-1} \text{ sec}^{-1}$.

Although (I) would seem to be of the proper magnitude for proton exchange, k_2 , which is four orders of magnitude less, appears much too small. Furthermore, from potentiometric titrations of the amide in water, it was found that the amide was ionized to a considerable extent at acidities where the exchange was still relatively slow. Why then, wasn't equilibrium (III) observed? The following sequence was postulated to explain these facts;



In the pH range of 0.8 to 2 $A \rightarrow B$ occurs to an appreciable extent but does not contribute to the measured rate of exchange. Therefore, the observed kinetics are for the equilibrium $A \rightarrow C$, which explains the small rate constant for (II). Furthermore, if C were present in small enough concentrations, equilibrium (III) would not be measurable. Significantly, in highly acidic solution where exchange is slow, the spectra did not show a triplet for the N-methyl resonance that would be expected from the $-NH_2^+CH_3$ form.

Later nuclear magnetic resonance studies of amides have led to a confirmation of these results. For example, Bunton, et al.,⁵⁶ measured the area under the N-H proton resonance for nine amides, including primary, secondary, and tertiary structures as a function of acidity and found no extra protons residing on the nitrogen, nor did they find a triplet resonance for the N-methyl protons at high acidities. Fraenkel and Franconi⁵⁷ estimated the barriers to internal rotation about the C-H bond following a procedure analogous to that discussed in Part II and found 12.7 kcal/mole for the N,N-dimethylformamide cation and 9.6 kcal/mole for the neutral molecule, which is again indicative of predominantly O-protonation. Interestingly, a temperature of 130° was necessary for the collapse of the N-CH₃ doublet in 100% sulfuric acid, while only 43° was necessary in an aqueous acid solution. This observation was taken as evidence for a rapid proton exchange at the nitrogen in aqueous solutions.

In rebuttal, E. Spinner⁵⁹ has proposed that the doublet observed for the N-methyl protons in N-mono-substituted amides is due to the protons on the methyl group being in slightly different environments; that is, the positively charged protonated nitrogen induces some double bond character into the N-C bond of the methyl group. However, as pointed out by Gillespie and Birchall⁶⁰ this hypothesis would require different areas for the N-methyl proton doublet, which has not been found for the N-monosubstituted amides studied thus far. Furthermore, E. Spinner raises the more valid question that if the amide oxygen protonates, why isn't an O-H band observed in the spectrum? All the earlier NMR workers had explained this away by assuming the O-proton exchange rate at room temperatures to be too fast for detection.

Recently, Gillespie and Birchall⁶⁰ have studied the NMR spectra of several amides in anhydrous fluorosulfuric acid^f from 25° to -90° C in an effort to slow the proton exchange rate sufficiently to allow detection of the protonated hydrogen resonance. In the spectrum of acetamide at 25° two peaks are observed which are not associated with the solvent or with the internal standard. The broad band at high fields was taken as that due to the NH₂ protons and the relatively sharp band at lower fields was assigned to the CH₃-C=O protons of acetamide. The peaks had relative areas of 2.04:3.00, respectively. At -80° the NH₂ resonance

^fBy a comparison of the melting points (-89°) this is apparently what the "Handbook of Chemistry and Physics" designates as fluorosulfonic acid (HSO₃F).

greatly sharpens and splits into a doublet (attributed to hindered rotation about the C-N bond), and a new absorbance appears as a shoulder on the solvent band. At -92° the new peak is completely resolved and the acetamide bands at this temperature have relative areas of 1.07:2.10:300, respectively, for the new peak, NH_2 and the CH_3 protons (the NH_2 absorbance was not further split at this temperature). Thus, the new peak was taken as the resonance band due to an OH proton.

For N,N-dimethylacetamide, the new peak appears at -79°C and is only 2.8 c.p.s. wide at this point, which indicates that the proton is more strongly bonded in this compound than in acetamide (this apparent increased basicity of the N-disubstituted derivative is compatible with the discussion in Part II). The relative peak areas at this temperature are 0.95:5.91:3.00, respectively, for the OH, $\text{N}-(\text{CH}_3)_2$ and $\text{CH}_3\text{C}=\text{O}$ protons. In this case, the new proton peak could arise from N-protonation, but, since the chemical shift was -9.80 ppm, while that in acetamide was -10.40 ppm, the authors conclude that the new resonance band was probably due to the OH proton in both cases. Similar results were obtained for formamide and its N-methyl derivative.

In summary, it appears that protonation of non-aromatic amides and lactams occurs predominantly at the oxygen. However, in most cases where it was possible to observe an effect, the nitrogen has shown some reactivity as well. Therefore, if a comparison of protonation and hydrogen bonding is indeed valid, an amide or lactam should preferentially hydrogen bond to the oxygen, and when conditions permit, show some additional contribution from the nitrogen.

CHAPTER II

EXPERIMENTAL

The Self-Association of N-Methyl-2-Pyrrolidone

To determine a self-association constant of a polar nonvolatile solute in a volatile solvent, three classical physical-chemical methods suggest themselves: i) isopiestic, ii) osmotic pressure, and iii) vapor pressure lowering. Isopiestic methods, which depend on the transfer of solvent between a source of known activity and a solution whose solvent activity is desired, are capable of high precision, but have the inherent disadvantage of slow equilibrium attainment. There are several ways to improve this situation, e. g., evacuation and rapid stirring, but at best it is still frequently a matter of weeks before equilibrium is attained. Osmotic pressure measurements, on the other hand, can be made somewhat more rapidly but reproducibility is perhaps more difficult due to the properties of the membrane. Vapor pressure lowering methods, however, are relatively rapid, attainment of pressure equilibrium is easily verified, and they are capable of sufficient accuracy in the range of equilibrium constants anticipated $(0.5 \text{ to } 2.0 \text{ (mole/l)}^{-1})$ to allow a valid determination. For these reasons, the last method was

the one chosen.

Apparatus

In designing a vapor pressure apparatus to use it was planned that various concentrations could be obtained from the same solution by simply evaporating successive portions of the volatile solvent. This method was particularly attractive since the vapor pressure of N-methyl-2-pyrrolidone (NMP) had been found to be only 0.31 ± 0.05 mm at 25°C . Therefore, assuming an ideal solution, and at a solute mole fraction of 0.05 (the highest required concentration) the partial pressure of NMP would be less than 0.02 mm of Hg at 25°C . Still another reason for trying this method was that an apparatus which had been used previously for water solubility studies could be readily adapted to this use.⁶⁸ This apparatus, depicted in Figure I, consists of two units connected by a mercury cup ball-joint which provides a grease-free, readily detachable seal. The lower portion consists of a 250 ml flask with a flat bottom to facilitate stirring. The upper portion of each unit is composed of a mercury manometer, a Teflon vacuum needle valve stopcock (Delmar Scientific Laboratories, Inc., Maywood, Illinois, ; \$14) fitted with Viton O-rings, and a mercury covered sintered glass disk which can be used for sample introduction to the evacuated system if needed.⁶⁸ The manometer was constructed from 18 mm O. D. tubing (approximately 16 mm I. D.) to render capillary depression of the mercury negligible.⁶⁶ Since the apparatus is fairly compact it is possible to immerse the entire

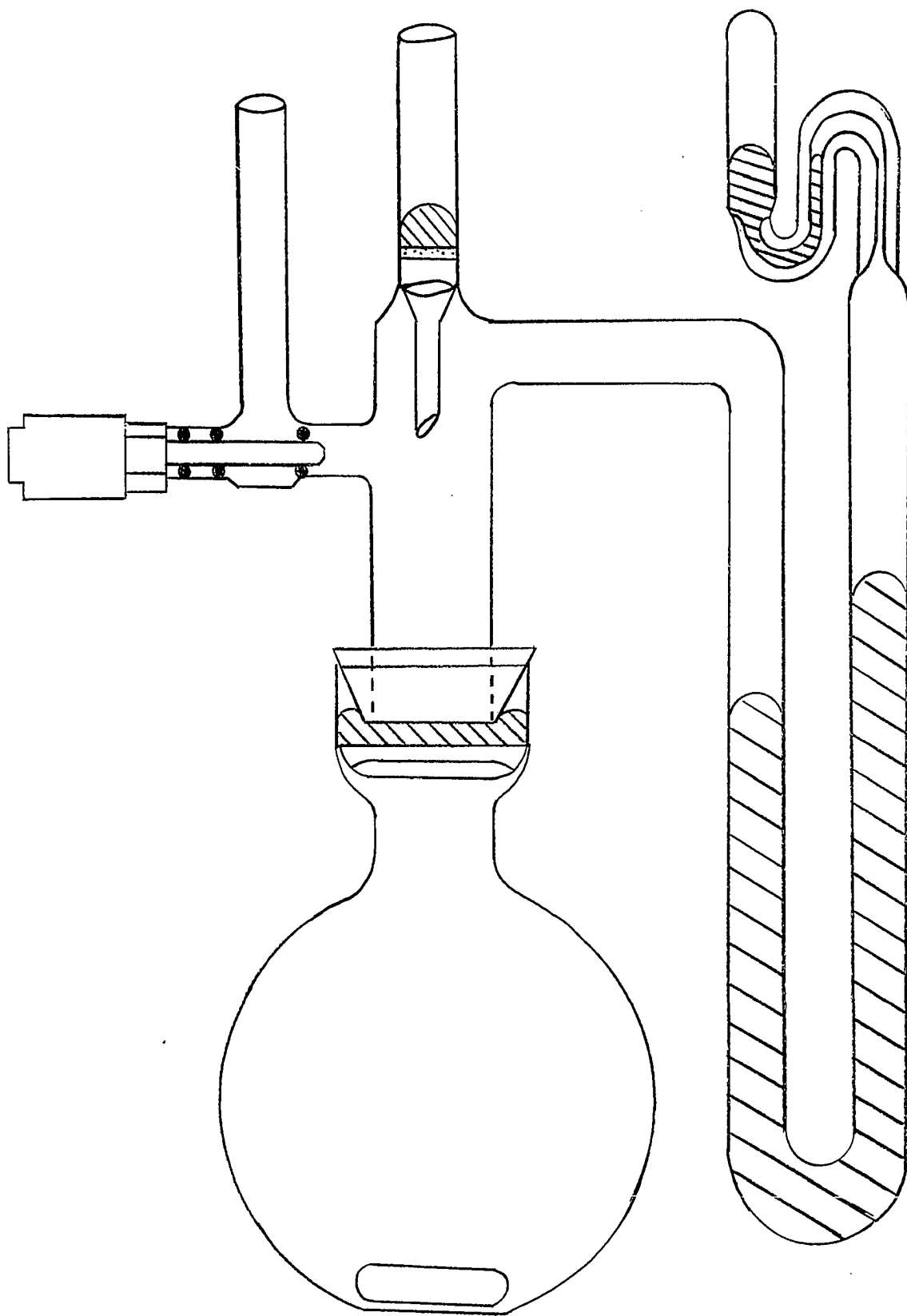


Figure I. The Vapor Pressure Apparatus. (Cross-hatching indicates Hg.)

assembly in a constant temperature bath, thus assuring a uniform sample temperature.

Constant Temperature Bath

A rectangular 20 gallon aquarium was used for a constant temperature bath (T.G. and Y.; \$15). An aquarium has at least two distinct assets as a constant temperature reservoir for vapor pressure work, since it is both made to hold water and to see through. The bath was provided with an evaporative cooler pump (Little Giant Corp., Oklahoma City, Oklahoma; approximately \$8) for stirring, a cooling coil, a 200-watt light bulb as a heat source and a thermo-regulator (Precision Thermometer and Instrument, Co., Industrial Park, Southhampton, Pa., Cat. No. T-260; \$65). (This particular regulator is the best mercury in glass temperature controlling device I have seen, and in connection with the Greiner Scientific electronic relay (Model No. E-3; \$55) which needs only 6 μ amp for activation, it should operate with dependability and accuracy for many years.) These components were arranged in the bath so that the flow from the pump passed successively over the cooling coil, light bulb, regulator and then the thermometer. With this arrangement, the regulator immediately senses the heat from the light bulb and slightly finer temperature control is obtained. Incidentally, the light bulbs were painted black or covered with aluminum foil to prevent glare and to provide a more even heat distribution. The temperature control provided with this equipment and arrangement was such

that very little change was detectable on a 0.01° division, 5.5 cm/degree thermometer. Therefore, the temperature was controlled within $\pm 0.01^{\circ}$ at 25°C . Further evidence for this precision of temperature control is that no variation in the pressure of carbon tetrachloride greater than the inherent error of the measurement (± 0.05 mm) was detectable over long periods of time.

Solvent and Solute Purification

To reduce any systematic error in the pressure measurements, the solvents and solutes were carefully purified. Eastman practical grade (apparently the only degree of purity readily available) N-methyl-2-pyrrolidone (NMP) was distilled through a 12-plate vacuum-jacketed Oldershaw column under reduced pressure at a rate of approximately 50 cc/hour. The boiling points obtained varied from run to run depending upon how well the joints were sealed, but they were never higher than 60°C , thus keeping any possible decomposition to a minimum. The product obtained in this manner had a refractive index of 1.4685 at 25°C as compared to the literature value of 1.469 at the same temperature.³⁷ Its density was 1.0290 at 26°C .

Usually, of the 500 ml of NMP distilled at a time a 150 ml middle fraction was retained for use. Immediately upon completion of the distillation the purified product was placed in a vacuum desiccator provided with drierite, evacuated, and stored in the dark. By storing the NMP in this manner, it was found that no detectable decomposition

occurred for months. Interestingly, impure NMP has a foul, dead-fish odor, but the distilled product is completely odorless.

Diphenylmethane was used as the solute in preparing ideal solutions in both carbon tetrachloride and benzene. The Matheson, Coleman and Bell practical grade product was vacuum distilled using the same procedure as for NMP, except that of the 500 ml added originally about the middle two-thirds was collected for use. In addition, the distilled product was recrystallized three times; the last two products had identical melting points of 25.4°C and refractive index of 1.5756 at 25°C as compared to the literature m.p. of $26-27^{\circ}$ and refractive index of 1.5768 at 20°C .⁶⁷

In the studies using carbon tetrachloride, the Baker and Adamson reagent grade product was successively scrubbed in a 4-liter separatory funnel with concentrated sulfuric acid, water, 20% potassium hydroxide, water and finally dried over anhydrous calcium sulfate (drierite), as suggested by Krchma and Williams.⁶⁵ The carbon tetrachloride was then refluxed over mercury in a hood for 2-4 hours to remove any sulfides and was distilled through a 30-plate vacuum jacketed Oldershaw column at a reflux ratio of 30:1. Out of the original two liters a forerun of 400-500 ml was discarded and approximately one liter of the solvent boiling at a constant uncorrected temperature of 75.5°C was collected for immediate use.

In preparing benzene for use as a solvent, the Fisher purified

product was distilled through an Ace Glass 27-plate bubble-cap column. From the original gallon a forerun of approximately 500 ml was taken at a reflux ratio of 30:1 and the main fraction, amounting to approximately 2.5 liters and boiling at a constant uncorrected temperature of $79.5 \pm 0.3^{\circ}$, was taken at a 10:1 reflux ratio.

Check of the Method

Turning to the actual vapor pressure determinations, at least two objections can be raised to the proposed method of solvent evaporation. First any non-volatile impurities present in the solvent would lower its apparent vapor pressure and second, any loss of the solute would give too high a pressure.

To reduce the possibility of the first objection being important the solvents were carefully purified as already described. Then, for benzene, a check was made for any possible effects from non-volatile impurities using the procedure outlined below. After weighing 100 ml of pure benzene into the 250 ml flask, small portions of the solvent were evaporated with an aspirator. To insure that all the evaporated solvent was caught, a double system was employed with each trap connected in series and immersed in a dry ice-acetone bath. Generally by just cracking the vacuum needle valve on the apparatus, approximately eight grams of the solvent would be removed in five minutes. At the end of the evaporation period the traps were removed and stoppered. After the solvent thawed, the traps were weighed, dried, and reweighed

to determine the amount of solvent removed. Usually the back-up trap contained less than 50 mg of the solvent. The data from this experiment are shown in Figure II as p vs. percent of benzene removed.

Two important points were illustrated in this graph. First it shows that the p° of benzene does not sensibly change even though the solution has been concentrated by a factor of three. Secondly, it can be seen that from 14-18% of the solvent must be removed before all the air and/or water is removed from the benzene (no effort was made to dry the solution beforehand). Therefore, when a run was made with solute present, no pressure readings were taken until at least 18% of the solution had been evaporated. It is important to note that the percentage of evaporation necessary for degassing probably depends upon the amount of solvent present, the rate of stirring, and to a lesser extent on geometry of the container. Furthermore, the percentage found from this experiment probably represents a minimum value, since only small quantities of solvent were removed at a time, thus allowing the air to reach an equilibrium state before further removal. Consequently, when a run was made with solute present, care was taken to reproduce these same conditions. The dashed line in the figure represents the average value of p° (95.06 Torr) obtained from all the pressure readings above eighteen percent.

A check was made of the purified carbon tetrachloride in a similar manner with the same type of plot shown in Figure III. The dashed

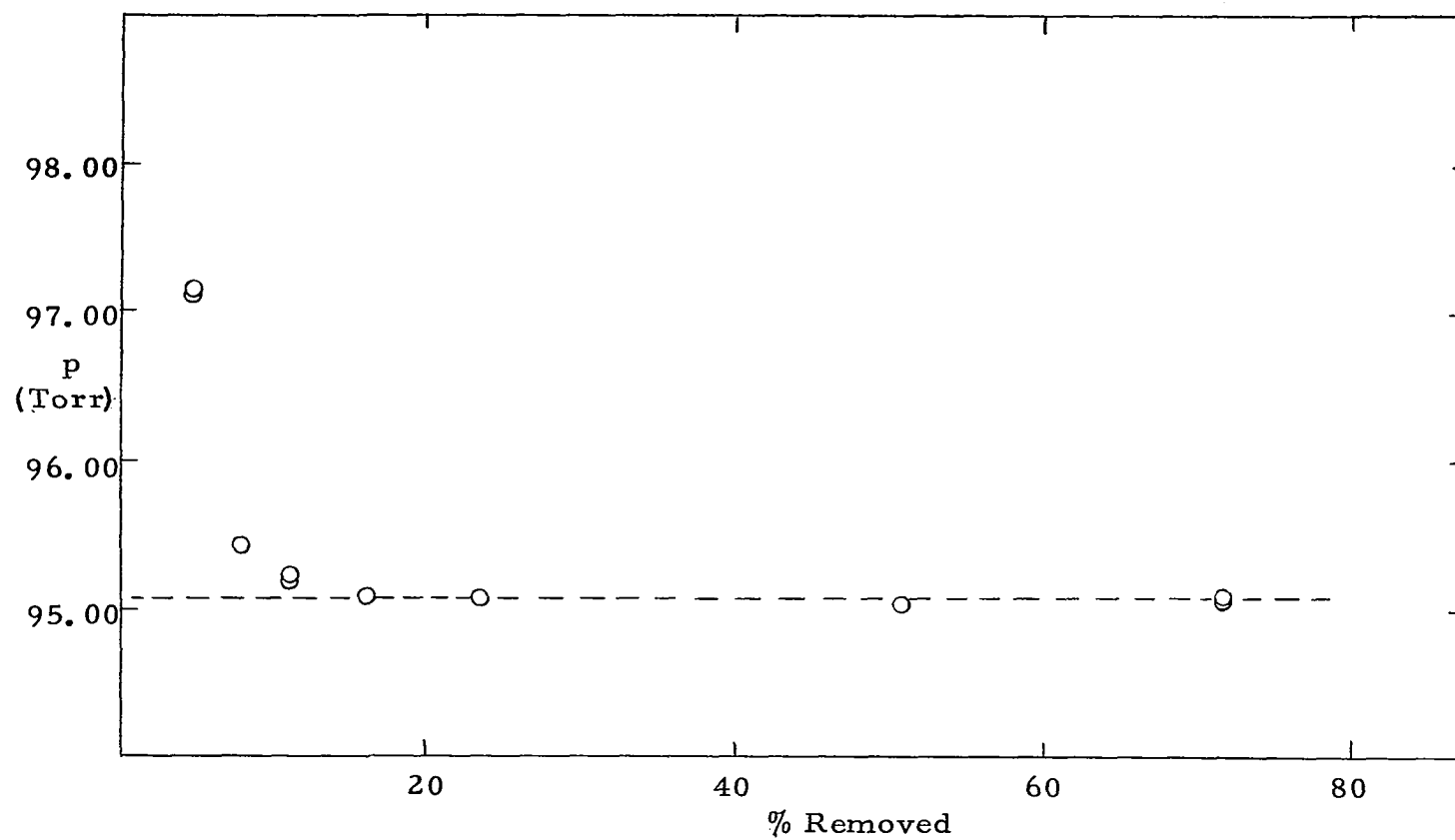


Figure II. Total Pressure as a Function of the Amount of Benzene Removed 25°C

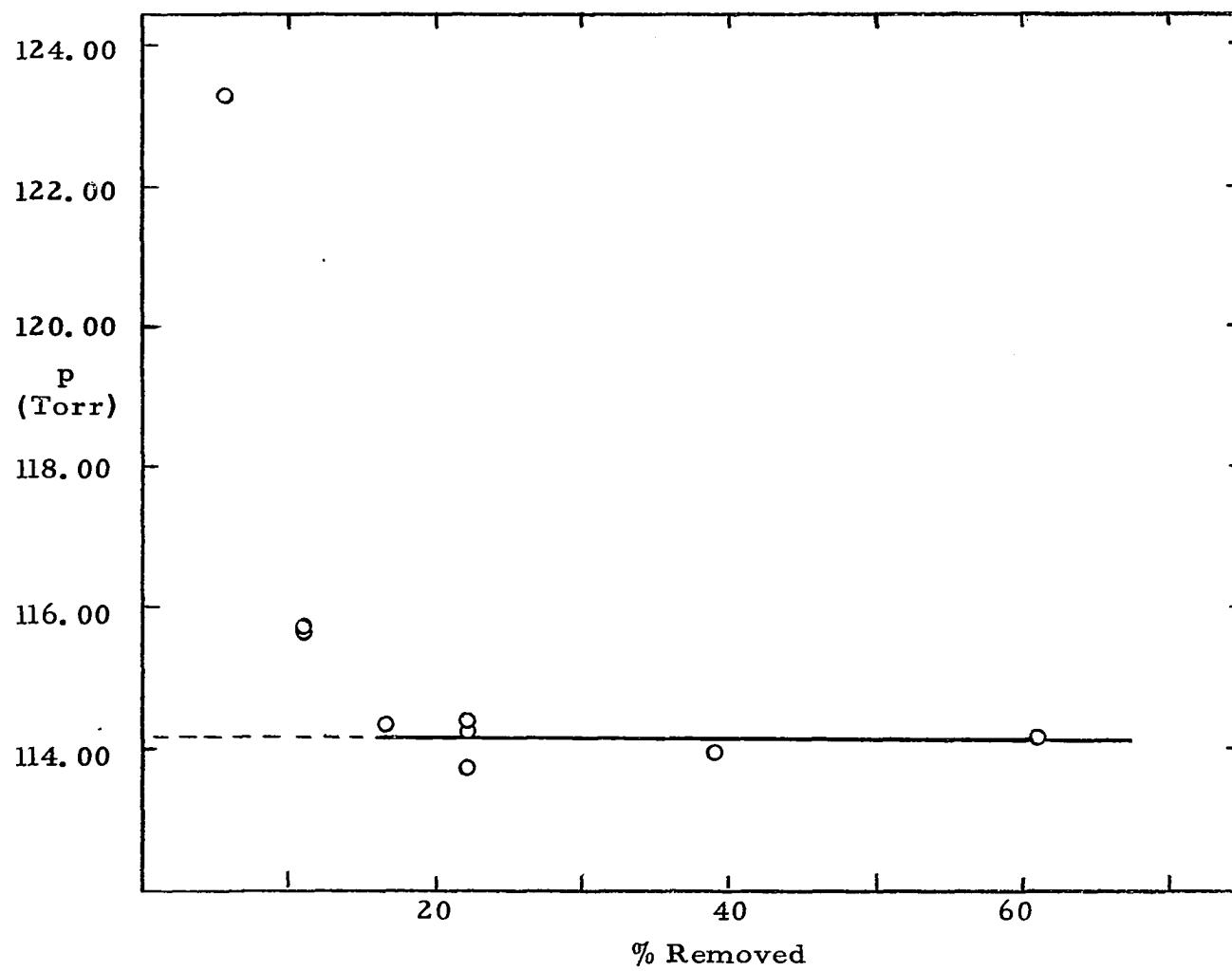


Figure III. Total Pressure as a Function of the Amount of Carbon Tetrachloride Removed 25°C

line in this plot is the average value of p° obtained from this and other determinations. In this experiment the percent removed was estimated from approximate volume marks on the flask. Again it is seen that p° changes only slightly more than the estimated experimental error of ± 0.05 mm over a 3-fold concentration of the solvent. As in the case of benzene, this plot shows that 15-20% of the pure solvent must be removed before the pressure due to air is negligible. The average value of p° found for carbon tetrachloride at 25°C was 114.08 mm Hg corrected to 0°C (actual average observed p° was 114.60 in mm of Hg at 25°C).

In order to check on the second possible objection to this method of obtaining vapor pressure lowering data, (loss of solute), a method of solute analysis was needed. Then, if loss occurred, the concentration could be corrected. Generally, the accurate determination of tertiary non-aromatic amides is difficult to accomplish, since they do not show a characteristic absorbance in a readily accessible spectral region and since their refractive indices are nearly identical with those of the common solvents, benzene, carbon tetrachloride, and 1,2-dichloroethane. However, advantage can be taken of the differences in the refractive index of NMP and water combined with the fact that the distribution ratio of NMP in carbon tetrachloride to that in water is about 0.03. Utilizing this information, standard solutions of NMP in carbon tetrachloride were prepared and aliquots of these were distributed with water in a ratio of two carbon tetrachloride to one water, thereby approximately

doubling the concentration in the water phase. From the standard plot a concentration of approximately 0.002 mole fraction of NMP in carbon tetrachloride could be detected.

Method

Fortified with an approximate method of analysis it was possible to proceed with the actual experiment. First a sample of dry NMP was rapidly weighed into the tared flask. Then 100 ml of solvent was added and the flask weighed again. (Due to the combined weight of the flask, stirring bar and solvent, it was necessary to make the last weight on a large solution balance.) After evaporating some of the solvent into the trap system to seat the mercury cup balljoint, the apparatus was immersed in the constant temperature bath. Additional solvent was removed with rapid stirring until 18-20% of the original amount had been taken off (this part requires a little practice since it is difficult to tell how much solvent is in the trap.) The amount removed was determined by weight and a portion of each condensate saved for analysis. Interestingly, when the solution had been completely degassed, only 10-15 minutes were required to reach pressure equilibrium, but if some air and/or water was present more than 30 minutes elapsed before the pressure became constant. However, even after complete degassing the pressure was not read in less than 30 minutes. This procedure was repeated until approximately 50% of the solvent had been removed. Subsequent analysis of the samples obtained in this way generally did not

show a detectable amount of NMP.

All pressure readings were made with a Gaerter Scientific Co. cathetometer (Model No. M 911, approximately \$265) equipped with a close-up lens attachment. It was possible with this optical system to focus on a mercury meniscus less than eighteen inches away, which gives a greater magnification, thereby improving the precision of the measurement. Furthermore, the manometer was constructed so that its arms were within 1/2 inch to minimize errors from the cathetometer not being level. By placing the manometer in front of the apparatus, the amount of water viewed through was reduced and a sharper image was obtained with the telescope.

Hydration of N-Methyl-2-Pyrrolidone and N,N-Dimethylacetamide

The Solute Isopiestic Method

The solute isopiestic method as applied to hydration studies has been described previously.^{69, 70, 71} Briefly, the apparatus consists of a suitable container, such as a wide-mouth Mason jar (available "anywhere" at \$1.65/doz. with lids), which is provided with a short section of glass tubing attached vertically to the outside. By slipping a metal rod, which is mounted vertically in the bath, through the glass tubing a means of both supporting and stirring the assembled apparatus in the constant temperature bath is obtained. Since the jar is free to rotate when mounted in this manner, stirring is obtained from the motion of

water in the bath. Inside the equilibrator, the constant water activity solution is placed in a beaker and the solution to be equilibrated is placed on the bottom of the jar.

Johnson's original apparatus was modified only slightly for the present application. First, the constant activity solution beaker was suspended instead of being placed directly into the organic solution. It was thought that mounting in this way would prevent any "creeping" of the sulfuric acid activity solution into the equilibrating solution. In addition, a practical advantage was also obtained by suspension, since less activity solution was needed even though large volumes of solution were used; that is, when 300 ml of solution are used, a large excess of constant activity solution would be necessary just to keep the beaker from floating. Secondly, the glass tubes were secured to the jar with electrical tape instead of epoxy resin. It was found that electrical tape provided a safe, inexpensive and rapid method of mounting the tubes that lasted for at least six months. The third major change in the basic apparatus as employed in this study was the use of polyethylene coated lids.^g After removing the rubber seal of the original Mason jar lid, a quarter-inch hole was drilled through it and a hook made from heavy copper wire was attached with solder. Then the lids were placed on greased aluminum foil which was in turn placed on a hot plate set at low heat. Strips of 1/32" sheet polyethylene were then melted over the lid

^gThis idea was first suggested by Robert Poor, to whom the author is indebted.

as to give one thickness over the entire surface and at least four thicknesses at the hole (2 on either side). After the polyethylene had melted sufficiently to adhere, the aluminum foil and lid were removed from the hot-plate and, while the plastic was still pliable, a jar was inverted over the polyethylene until it resolidified. The last step was taken to provide a good seal. Next the polyethylene covering the 1/4" hole was drilled out with a cork borer to fit a small ground glass stopper. Although the procedure sounds complicated, a person can easily prepare twenty-four lids in an eight hour period.

The sealing of the isopiestic cells with polyethylene coated lids has at least two distinct advantages over the saran wrap-aluminum foil method employed earlier; 1) once made, the lids can be reused and rapid equilibrators assembly is possible, and 2) the ground glass stoppers provide an easy method of resealing the apparatus after a sample has been removed.

Solvent and Solute Purification

Reagent Grade carbon tetrachloride and benzene were further purified by distillation through either a 27-plate bubble-cap or a 30-plate vacuum jacketed Oldershaw column as described in Part I. The Matheson, Coleman and Bell technical grade 1, 2-dichloroethane was scrubbed with concentrated sulfuric acid until no further discoloration of the acid phase was noted. (Usually, three batches were sufficient.) Then it was successively scrubbed with water, twenty percent sodium

hydroxide, and again with water. Finally the dissolved water was removed with anhydrous calcium chloride and the product distilled through the Oldershaw column described previously. A fraction boiling at a constant uncorrected 81.5°C , which amounted to most of the sample, was collected for use.

N-methyl-2-pyrrolidone was purified and stored as described earlier. The N,N-dimethylacetamide as obtained from K and K Laboratories was apparently in a high state of purity since it was clear, odorless and had a refractive index of 1.4359 at 25°C which compares favorably with the value of 1.4359 obtained by Meighen and Cole⁷² after careful purification. Therefore, this sample was not further purified. It was, however, dried before use by storage for a week in an evacuated desiccator which was provided with anhydrous calcium sulfate and protected from any direct light.

Preparation and Use of the Constant Water Activity Solutions

The constant water activity solutions were prepared using Mallinckrodt Analytical Reagent grade concentrated sulfuric acid without further purification. Water activities of the solutions were obtained in the following manner. A double plot of water activity vs. molality as given by Robinson and Stokes⁷³ and density vs. molality as obtainable from the "Handbook"⁷⁴ was made from which activity vs. density could be obtained. All densities were measured on a density balance calibrated with water at 25°C . It was found that this balance would reproduce a

density to within ± 0.0003 g/ml. Table V lists some relationships useful in obtaining approximate activities which, of course, can later be determined accurately by measuring the density.

TABLE V
APPROXIMATE RATIO OF COMMERCIAL CONCENTRATED
SULFURIC ACID ($\rho = 1.833$) TO WATER FOR
VARIOUS ACTIVITIES

a_w	Expected ρ at 25°C	ml of H ₂ SO ₄ /ml of water
0.950	1.075	155/2000
0.850	1.166	314/1720
0.700	1.249	472/1600
0.550	1.314	620/1500
0.400	1.378	755/1375

Generally between 30-40 ml of the constant activity solution was used per equilibrator cell. Since the organic solution volume was less than 200 ml and the total water concentration was less than 0.1 mole/liter, only about 0.4 g of water were transferred. The loss of this amount of water does not detectably change the activity of 30-40 ml of the acid solution.

Preparation of the Solutions

All samples were prepared in an identical manner. First, an approximate quantity of dry NMP was rapidly pipetted into a tared 50 ml beaker and weighed immediately. The pipet used for this purpose was a

graduated 5 ml pipet with a sawed off tip. During the 2-3 minutes necessary for this operation it was found that no more than one mg of water was absorbed by the sample. Therefore, even for the smallest sample, which was about 5 g, the error due to water was quite negligible. Next the weighed sample was quantitatively transferred to a 500 ml volumetric flask with the solvent under study. Whether or not the sample took up water after it was weighed was of no consequence, since the activity was to be adjusted in the equilibrators jars.

These standard solutions were then divided among the equilibrators which were sealed immediately to minimize any evaporation. Five or six of the 25 jars were randomly chosen and weighed on the solution balance. Twenty-four hours prior to sampling and after five days of equilibration these same samples were reweighed to check for loss of solvent. The worse loss ever recorded was approximately 3 grams out of 170, or about two percent. However, in general, the loss of solvent was less than one percent, which is at least as accurate as any method of analysis conceived for this lactam.

Equilibration of the samples was allowed to proceed for six days as indicated above. Christian, et al.,⁶⁹ and Johnson⁷¹ have shown that vapor phase equilibration of water between a constant activity solution and solvents of low solubility is amazingly rapid. For example, pure benzene which dissolves 0.036 mole/liter of water at 25°C, attains an effective equilibrium in about 12 hours in the apparatus described

above. With a hydrating solute present, however, attainment of equilibrium will be slower. But, even at the highest solute concentrations used, a total water concentration of only 3 to 4 times that which would dissolve in the pure solvent was observed. Therefore, in the case of benzene an equilibration time of only 36 to 48 hours should be sufficient (the equilibration time would be even less for carbon tetrachloride). Applying a similar argument to the hydration studies in 1, 2-dichloroethane (DCE) the minimum time required for equilibrium would be about 70 to 100 hours, since it requires approximately 36 hours to reach water equilibrium with pure DCE, and since the highest water concentration with solute present was only 2 to 3 times that of pure DCE. In any event the samples were always left 5 days for the CCl_4 and 6 days for benzene and DCE solutions to assure the attainment of a practical equilibrium. Additional evidence for equilibrium having been reached was obtained from the titration of one or more samples 12 to 18 hours after their initial determination. In every case the initial results was reproduced to within experimental error.

To facilitate equilibration the samples were allowed to swing freely about their support rods in the bath. At least twenty-four hours prior to sampling, however, the jars were clamped down so that the water level came up to the lid. Even though this prevents further agitation, it would tend to eliminate any temperature variations throughout the equilibrator. Nearly total immersion was particularly important

for the 15 degree work where there was a 10 to 15°C differential from the room temperature. Furthermore, the cells were left clamped while sampled for the same reason.

Constant Temperature Bath

An 8x2x1 foot sheet metal tank supported two feet from the floor was especially designed for the solute isopiestic method. Two inserts, each consisting of two pieces of sheet metal separated by four inch spacers and with corresponding one-quarter inch holes drilled at the corners of four inch squares over their surfaces, were placed in the tank. Three-sixteenths-inch diameter welding rods, about ten inches in length, were slipped through the matching holes of the inserts to act as equilibrator supports. The entire bath with inserts was coated with epoxy paint to minimize corrosion (epoxy paints are apparently stable indefinitely under water but have low resistance to abrasion).

Adequate stirring is essential for good temperature control. To this end, the tank was equipped with two Little Giant evaporative cooler pumps located midway on either side and pointing in opposite directions. This method imparted vigorous motion to the water and temperatures were found to vary no more than $\pm 0.02^{\circ}\text{C}$ throughout the bath at a given time. Temperature control was provided by the mercury-in-glass regulator and electronic relay system described elsewhere.

In general, and even for weeks at a time, the temperature varied less than $\pm 0.05^{\circ}\text{C}$ with this arrangement.

Titration

All water titrations were performed using the Karl Fischer method with an automatic Beckman KF-3 Aquameter. This instrument operates on a semi-dead-stop end-point principle utilizing the fact that water in an inert solvent, e.g. methanol, polarizes the platinum electrodes. Thus, when an equivalent amount of Karl Fischer reagent has been added there is a sharp drop in the resistance of the electrode unbalancing the bridge circuit which closes the titrant valve. This method is only a semi-dead-stop method since the actual end-point is somewhat arbitrary because there is a slow drift with time. Therefore, in all the titrations reported here, and indeed in the laboratory, a value of 30 seconds was chosen as a standard. One other point worth mentioning in regard to the end-point is that it varies slightly with the rate of delivery.

In any event, every effort was made to reproduce the conditions from run to run, with particular emphasis of the rate of delivery, position of the electrode, and rate of stirring. In general, this method was found to give quite satisfactory reproducibility (see for example Figures VIII and IX).

The Karl Fischer reagent was prepared and standardized by the methods of Taylor⁷⁵ and Johnson.⁷¹ Along with each standardization a unit activity sample from a previous run was repeated. Generally, the agreement from run to run was within 2 percent. Table VI shows

the solubility of water in carbon tetrachloride, and benzene and DCE as determined from several independent standardizations. All unit activity water solubility samples for solvents with densities greater than 1 g/ml were obtained using a "lens" technique. This method utilizes the fact that the cohesive energy of water is such that when 25 ml of distilled water are placed on top of a much larger amount of solvent in an erlenmeyer, the water forms a ring around the flask. Thus, a sample of the water saturated organic solvent can be easily removed for titration from the center of the flask without fear of contamination.

TABLE VI
SOLUBILITY OF WATER IN CARBON TETRACHLORIDE,
BENZENE AND 1, 2-DICHLOROETHANE (DCE) 15°C

Run	f_w^0 (mole/liter)		
	CCl ₄	Benzene	DCE
I	0. 00574	0. 02601	0. 0970
	0. 00584	0. 02601	0. 0980
	0. 00589	0. 02605	0. 0970
II	0. 00573	0. 02582	0. 0928
	0. 00588	0. 02586	0. 0929
III		0. 02553	0. 0937
		0. 02553	0. 0931
		0. 02566	0. 0932
IV		0. 02607	
		0. 02600	

CHAPTER III

TREATMENT OF THE DATA AND RESULTS

Self-Association of N-Methyl-2-Pyrrolidone

As described in the experimental chapter, the extent of self-association of N-methyl-2-pyrrolidone (NMP) in carbon tetrachloride and benzene was inferred from vapor pressure lowering data. The measured quantities obtained with this method are formal (analytical) concentration, X_f , and p , the observed pressure. The observed pressure is really a total pressure; however, it is taken as the partial pressure of the solvent since the pressure of NMP above an ideal solution is less than 0.02 mm at 25°C even for the highest concentrations.

A value of p_1^0 for carbon tetrachloride of 114.08 ± 0.05 Torr at 25°C was obtained as described in Chapter II and illustrated in Figure III. This value is in good agreement with the 114.05 Torr calculated from the Antoine equation bracketing this temperature as given by Weissberger, et al.⁷⁶

Vapor pressure data for concentrations of diphenylmethane (DPM) between 0.02 and 0.04 mole fraction are given in Table VII.*

* All Tables and Figures referred to in this chapter are assembled in numerical order between pages 73 and 124.

Figure IV shows a plot of p vs. X_{DPM} , the expected ideal pressure lowering is indicated by the solid line. As can be seen, diphenylmethane appears to behave ideally in this concentration region. Table VII also contains the apparent molecular weights of DPM calculated for each experimental point. These molecular weights were obtained from the following relationships, by assuming Raoult's law to be obeyed and remembering that $X_1 + X_2 = 1$;

$$p_1 = X_1 p_1^{\circ} = (1 - X_2) p_1^{\circ}$$

where "2" refers to the solute. Rearranging

$$p_1^{\circ} - p_1 = X_2 p_1^{\circ}$$

or

$$X_2 = \frac{p_1^{\circ} - p_1}{p_1^{\circ}} = \frac{\Delta p}{p_1^{\circ}}$$

but

$$X_2 = \frac{g_2/M_2}{g_2/M_2 + n_1}$$

where M_2 is the molecular weight of the solute and n_1 is the number of moles of solvent.

Therefore,

$$M_2 = \frac{g_2}{n_1} \cdot \frac{p_1^{\circ} - \Delta p}{\Delta p} = \frac{g_2}{n_1} \cdot \frac{p}{\Delta p} \quad (3-1)$$

Equation (3-1) gives the apparent molecular weight directly in terms of the measured quantities g_2 , n_1 , p and Δp (g_2 and n_1 were determined from

weighed quantities). As indicated in the table the average apparent molecular weight, 167.3 ± 3 g/mole, agrees reasonably well with the theoretical value of 168.23 g/mole. The agreement is sufficient to conclude that the measured p_1^0 is nearly correct for the solvent used.

Vapor pressure lowering data for NMP in carbon tetrachloride are summarized in Table VIII. The solvent partial pressures reported in this table are for a concentration range of 0.01 to 0.05 mole fraction of NMP. Figure V shows a plot of p vs. X_{NMP} for the data given in the Table. The solid line in this illustration indicates the pressure lowering expected for an ideal solution. It is apparent from this plot that NMP in carbon tetrachloride shows a positive deviation. Assuming that the solute obeys Henry's law over the concentration range studied (up to 5 mole percent), a positive deviation may be explained by solute-solute association. Furthermore, a self-association constant may be inferred from the extent of positive deviation. Assuming in addition only monomer-dimer equilibrium to be involved,



an equilibrium constant for reaction (3-2) may be obtained. The formal concentration of NMP may then be expressed as

$$X_f = \frac{n_M + 2n_D}{n_M + 2n_D + n_s}$$

where n_M and n_D are the moles of monomer and dimer, respectively, n_s is the number of moles of solvent. X_f , however, is an analytical

concentration, while the concentration inferred from pressure measurements is an apparent mole fraction. Therefore, to properly evaluate an equilibrium constant the formal concentration must be put on an apparent basis.

Since,

$$X_a = \frac{n_M + n_D}{n_M + n_D + n_s} = X_M^a + X_D^a = X_M^a + K_{20} X_M^{a^2},$$

where K_{20} is the equilibrium constant for reaction (3-2), it can be seen that X_f may be converted to an apparent scale by dividing top and bottom of the formal relationship by $n_M + n_D + n_s$. Thus,

$$X_f = \frac{n_M + 2n_D}{n_M + n_D + n_s} \div \frac{n_M + 2n_D + n_s}{n_M + n_D + n_s} = X_M^a + 2X_D^a \div 1 + X_D^a$$

or,

$$X_f = \frac{X_M + 2K_{20}X_M^2}{1 + K_{20}X_M^2},$$

where the superscript "a" has been dropped since all future uses of species concentrations will be taken on an apparent basis.

Now that the mole fractions have been placed on a basis meaningful to colligative property measurements, it will be possible to proceed with the data analysis. Since the concentrations were determined by weight they are known more accurately than are the pressures and in particular the Δp values. Therefore, a proper least squares treatment of vapor pressure lowering data would place all the uncertainty in

the pressure data.

$$\Delta p = X_a p_1^o = (X_M + X_D) p_1^o = (X_M + K_{20} X_M^2) p_1^o \quad (3-4)$$

Although K_{20} could be expressed in terms of the measured quantities, X_f and p , by eliminating X_M from equations (3-3) and (3-4), it would be found that Δp was not a linear function of the dimer constant. Therefore, we are confronted with the problem of both placing the error in Δp and solving a non-linear least squares analysis problem to find the best value of K_{20} .

The procedure used to find a least squares value of K_{20} is outlined below. First a trial value of K_{20} , obtained graphically, was used to calculate X_M from equation (3-3) point by point. Then using these initial values of X_M , solvent partial pressures were calculated from equation (3-5) for each datum.

$$p_i \text{ (calc)} = p_1^o - (X_{M_i} + K_{20} X_{M_i}^2) p_1^o \quad (3-5)$$

From each $p_i \text{ (calc)}$ a term in expression (3-6) was obtained.

$$E = \sum_i^n (p_i - p_i \text{ (calc)})^2 \quad (n = \text{number of data points}) \quad (3-6)$$

The entire procedure is then repeated until a minimum in E , the error, is found.

An iterative procedure such as this is readily adaptable to digital computer techniques. In order to reduce the trial and error portion of the technique outlined above, three values of E were obtained from

the initial guess for K_{20} , and from its incremented and decremented values (0.5 percent). Using the three E values thus obtained and assuming the error contour to be parabolic, the location of the minimum can be easily estimated. The next value of K_{20} used was therefore the value at the calculated minimum in the error contour. With this method convergence is very fast, particularly since the parabolic assumption improves as the actual minimum is approached. In reality, however, the data were fit as a two parameter problem, since reliable values of p_1^0 are difficult to obtain by static methods. In the two parameter treatment of the pressure data the method outlined above was repeated for three values of p_1^0 . One least squares fit was found for the experimental p_1^0 and two others from this value incremented and decremented by 0.1 mm. From the errors associated with these three minima the overall minimum was calculated.

The above treatment yielded values of $K_{20} = 0.71 \pm 0.06$ (mole/liter)⁻¹ converted to a molar basis, and $p_1^0 = 114.04 \pm 0.03$ Torr and an overall root mean square deviation (RMSD), defined as,

$$\sqrt{\frac{\sum_i^n (p_i - p_i(\text{calc}))^2}{(n - p)}}$$

where p is the number of parameters, of 0.08 units of p. The errors given with the parameters represent one- σ values and were calculated according to the method of Christian.⁷⁸ The dashed line in Figure V corresponds to the pressure-concentration relationship calculated from

the above parameters.

For benzene the value $p_1^0 = 95.07$ Torr at 25°C was obtained as discussed in the experimental section. The vapor pressure lowering data for DPM in benzene is shown in Figure VI. As for the same solute in carbon tetrachloride, the apparent molecular weights for each experimental pressure were calculated from equation (3-1) and are listed along with the experimental data in Table IX. The average value of 169.0 ± 2.4 g/mole is in fair agreement with the theoretical value of 168.23 g/mole for DPM, thereby indicating that p_1^0 is approximately correct for the sample of benzene used.

The vapor pressure data obtained for concentrations of NMP between 0.01 and 0.05 mole fraction were treated identically with those for carbon tetrachloride. The raw data and calculated values are given in Table X. A dimerization constant of 0.39 ± 0.03 (mole/liter) $^{-1}$ and a p_1^0 of 95.13 ± 0.02 Torr at 25°C were found using this method. These parameters fit the experimental data to an overall RMSD of 0.07 units of p . Although the calculated value of p_1^0 for benzene agrees with the 95.22 Torr calculated for the same temperature from the Antoine equation given by Weissberger,⁷⁷ the experimental value differs by 0.16 mm of Hg. However, what is more important to the present application is that the calculated and experimental values differ by only 0.06 mm of Hg, which is just slightly beyond the estimated error of ± 0.05 mm. The relationship between p and X_{NMP} is illustrated in Figure VII, where the

dashed line is the expected behavior based on the calculated p_1^0 and K_{20} values given above.

Solubility of Water in the Pure Solvents

The solubility of water in carbon tetrachloride at 25°C found for various water activities (a_w) is given in Table XI. Included in this table are solubilities predicted at the same activities using Johnson's⁷¹ value of 0.0087 mole/liter for C_w^0 , the reciprocal Henry's law constant for monomeric water; that is, the solubility at unit water activity. As can be seen, the data obtained in connection with this study are in good agreement with the predicted values. Therefore, $C_w^0 = 0.0087$ mole/liter was accepted for use with the hydration studies in carbon tetrachloride at 25°C.

Table XII gives the same type of data for the solubility of water in carbon tetrachloride at 15°C. Since the solubility of water at 15°C had not previously been reported from this laboratory, a plot of f_w^0 , the formal water concentration, vs. a_w was prepared. Plotted in this manner, it was apparent that within the estimated experimental error of ± 0.0005 mole/liter a linear relationship exists between water solubility and activity in carbon tetrachloride at 15°C. The latter results indicate that water exists primarily as the monomer in carbon tetrachloride at this temperature as it does at 25°C.⁶⁹ A standard least squares treatment assuming a_w to be free of error and the errors in f_w^0 to be normally distributed, gave $C_w^0 = 0.0057$ mole/liter. A comparison of the

experimental water solubility and those calculated from $f_W^0 = 0.0057$ (a_W) are also given in Table XII.

Solubilities of water at several activities in pure DCE at 25° and 15°C are reported in Tables XIII and XIV, respectively. Plots of f_W^0 vs. a_W for both temperatures show a definite positive curvature, which agrees qualitatively with the relationships found by Johnson⁷⁹ at 25° and 10°C. However, the average value at 25°C for $a_W = 1$ is about 3% higher than previously reported. Therefore, if the same species (monomer-trimer) and equilibrium constant is assumed for the 25°C data, a C_W^0 of 0.110 mole/liter is obtained, which is only slightly higher than the value of 0.1083 ± 0.0007 mole/liter reported earlier. Treating the 15°C data similarly, but using the trimer constant, $K_{30} = 12 \text{ (mole/liter)}^{-2}$, interpolated from Johnson's 10 and 25°C data combined with Lin's⁸⁰ 35°C work, a C_W^0 of 0.080 mole/liter was found, which is in reasonable agreement with the interpolated C_W^0 of 0.079 mole/liter.

Values of f_W^0 calculated from

$$f_W^0 = C_W^0 a_W + 3K_{30} (C_W^0 a_W)^3$$

using the respective C_W^0 and K_{30} values for 25° and 15°C are offered for comparison in Tables XIII and XIV.

A plot of f_W^0 vs. a_W for water in benzene at 15°C surprisingly showed a slight positive curvature, which indicates the presence of water species other than monomer. Since the solubility of water as a function of activity at 15°C had not been previously determined in this laboratory,

the solubility measurements were repeated as indicated by the circles and squares in Figure VIII. Noting that the agreement was satisfactory, the combined data were subjected to a standard least squares treatment using the following relation, where the solute has been assumed to obey Henry's law,

$$f_W^o = C_W^o a_W + mK_{mo}(C_W^o a_W)^m + nK_{no}(C_W^o a_W)^n$$

and letting m vary from 0 to 4 and n from 0 to 6. All the least squares solutions together with their respective overall RMSD for each set of species tried is compiled in Table XVI. Application of the formula;⁹⁷

$$\Delta \text{RMSD} = \frac{0.477 \text{ RMSD}(\min)}{(n - p)^{1/2}} \quad (3-7)$$

which gives information regarding the statistical significance of a change in RMSD with the number of parameters, indicates an increase (with $n = 38$, and $p = 2$) of 8 percent in any RMSD value above RMSD(min) would be evidence against that particular set of species. Applying the same argument in another direction, it can be stated that if the addition of another parameter does not give a decrease of 8 percent in RMSD then the new fit is not statistically superior. It can be seen from the values of RMSD listed in Table XVI, that assuming only monomers does not lead to a satisfactory fit and also that no three-parameter fits, which have all their constants positive, give a statistically significant decrease in the overall error. Furthermore, of the three possible two parameters fits considered physically reasonable only the monomer-tetramer species

may be excluded on purely a statistical basis. Thus, only two sets of water species would seem to adequately explain the solubility data in benzene at 15°C; monomer-dimer and monomer-trimer. Noteworthy is the fact that C_W^O changes less than 6% for all the physically significant cases. The equilibrium constants associated with these species are; $K_{20} = 3.8 \text{ (mole/liter)}^{-1}$ and $K_{30} = 67 \text{ (mole/liter)}^{-2}$. A trimer constant of this order of magnitude implies a species concentration of only 0.0009 mole/liter, which contributes 0.0026 mole/liter to the formal concentration, or stated another way, the polymerized water contributes about 10% to the analytical concentration. The solid line in Figure VIII is for the trimer fit and the dashed line indicates the change in the monomer concentration with activity. Table XV shows the solubility of water in benzene at 15°C as a function of a_W , and f_W^O values calculated from $K_{30} = 67 \text{ (mole/liter)}^{-1}$. By way of comparison of water solubilities in benzene at 15°C, Taylor⁹⁸ reported $f_W^O = 0.0265 \text{ mole/liter}$, Moule and Thurston,⁹⁹ $f_W^O = 0.0261 \text{ mole/liter}$ both of which agree well with the least squares value of 0.0260 mole/liter reported here.

The data obtained for the solubility of water in benzene at 25°C are depicted in Figure IX and compiled in Table XVII. Similar to the system water-benzene at 15°C, there is a slight positive curvature in the f_W^O vs. a_W plot and the data were reproducible. However, since this slight curvature had not been noted by previous investigators, a careful check for possible systematic errors was made. In the second determination

of the solubility of water in benzene at 25°C , at least five items of the experimental technique were varied: 1) the constant activity solutions were placed on the bottom of the equilibrator cell in tall form 200 ml beakers, 2) the equilibrators were immersed up to the lid in the constant temperature bath for the duration of the experiment, 3) some of the sulfuric acid activity solutions were replaced by corresponding calcium chloride solutions, 4) newly-prepared sulfuric acid solutions were used at some activities and 5) different sample sizes were used for the second set of titrations. The data from this second run are distinguished from the first in Figure IX by squares for sulfuric acid activity and hexagons for calcium chloride activity solutions. Generally the agreement was satisfactory and either together or separately both runs show the same slight positive curvature. Therefore, all the data were used for the least squares analysis as described for water in benzene at 15°C .

In Table XVII the raw data are reported for the solubility of water in benzene at 25°C and in Table XVIII a comparison of the least squares fits assuming various species. Using the method of analysis that was applied to water in benzene at 15°C , it can be seen that once again none of the three-parameters fits tried shows a significant improvement over two-parameter cases. Contrary to the 15°C case, however, the monomer-dimer assumption appears to be statistically inferior to the monomer-trimer and monomer-tetramer assumptions. Perhaps significantly, the only two parameter fit which satisfies both the 15° and

25°C water data in benzene is that corresponding to a monomer-trimer species. The trimer equilibrium constant is $32 \text{ (mole/liter)}^{-2}$ and C_W^0 is 0.0330 mole/liter. Thus, at 25°C and unit water activity there would be a trimer concentration of 0.0012 mole/liter, which contributes 0.0035 mole/liter to the formal concentration. Note that although the 25°C trimer constant is only one-half the value at 15°C the trimer concentration is slightly greater, a fact which reflects the greater water solubility at 25°C. For comparison, the unit activity solubility value of 0.0365 mole/liter found in this study is in fair agreement with the values of 0.0365,⁷⁵ 0.0359,⁹⁹ and 0.0347⁷⁰ mole/liter reported in Literature. (However, for a comprehensive discussion of water solubilities in benzene see references 75 and 71.)

Hydration Studies

The hydration data for NMP and N,N-dimethylacetamide in all solvents systems ~~were~~ treated identically. Therefore, the treatment of the data will be discussed generally.

From the method of hydration study employed, the measured quantities are: f_W , the formal concentration of water in the solvent-solute systems; f_A , the formal concentration of lactam or amide; and f_W^0 , the solubility of water in the pure solvent at the same activity. Thus, assuming a set of species and that the individual species obey Henry's law over the concentration range studied (less than 5 mole percent), f_A may be expressed as follows;

$$f_A = \sum_{i,j}^n (i)K_{ij}C_A^i C_W^j \quad i \neq 0 \text{ and } K_{10} = 1$$

and

$$f_W = \sum_{i,j}^n (j)K_{ij}C_A^i C_W^j \quad j \neq 0 \text{ and } K_{10} = 1$$

where C_A and C_W are the monomer concentration of lactam or amide and of water, and K_{ij} is the formation constant for species A_iW_j . In principle the upper limit of this summation could be any value of n , but from consideration of the type of interactions and the low concentrations of the associating molecules it seems reasonable to limit n to 2 or 3 for the initial attempts at curve fitting the hydration data. Another point that should be made before the discussion of the data treatment technique is begun is that the formal concentration of water with solute present will always be expressed as Δf_W , the bound water. This quantity is obtained simply by subtracting the amount of water dissolved in the pure solvent, f_W^0 , at a given activity from the formal water concentration, f_W , found for a given solute concentration at the same activity. Thus,

$$\Delta f_W = \sum_{i,j}^n (j)K_{ij}C_A^i C_W^j \quad i \text{ and } j \neq 0$$

Plots of Δf_W against f_A were qualitatively similar for all seven systems studied in that a pronounced positive curvature was apparent. However, the curvature decreased in the order, carbon tetrachloride, benzene and DCE as illustrated in Figures XI through XVII. A positive curvature in a plot of this type indicates that species other than monomer-

monohydrate (AW) are present in detectable concentrations. Further inferences can be reached from these raw data graphs. For example, the positive curvature may be due to the formation of a monomer-dihydrate (AW_2), or to the formation of a monohydrate of a higher order NMP species, such as, a dimer-monohydrate (A_2W). Ignoring for the moment the effects of the self-association of NMP, the latter possibility may be checked graphically. If only AW and A_2W species are present then;

$$f_A = C_A + K_{11}C_A C_W + 2K_{21}C_A^2 C_W$$

and

$$\Delta f_W = K_{11}C_A C_W + K_{21}C_A^2 C_W$$

Therefore,

$$f_A = C_A + \Delta f_W + K_{21}C_A^2 C_W$$

or

$$C_A \cong f_A - \Delta f_W$$

Then

$$\Delta f_W = K_{11}(f_A - \Delta f_W)C_W + K_{21}(f_A - \Delta f_W)^2 C_W$$

or alternately

$$\Delta f_W = K'_{11}(f_A - \Delta f_W)a_W + K'_{21}(f_A - \Delta f_W)^2 a_W$$

Since

$$C_W = C_W^0 a_W \quad \text{and} \quad K'_{11} = K_{11}C_W^0$$

Consequently, if the above assumption is correct, a plot of Δf_W vs. $(f_A - \Delta f_W)a_W$ should be a single line showing a positive deviation for all the

water activities, a_W , studied. This plot is shown in Figure X for NMP in carbon tetrachloride at 15°C. It can be seen that the data do nearly form a single line and that no appreciable systematic trend for different activities is detectable. The latter observation may be taken to mean that a dihydrate species does not make a large contribution to Δf_W in carbon tetrachloride. Similar plots for NMP in benzene and DCE generally show the same behavior except that systematic deviations among the various activities become more apparent, particularly with the studies in the latter solvent.

Graphical estimates such as this are essential to obtain a basis for subsequent numerical analysis techniques. Thus, the initial relationships used for curve fitting were;

$$f_A = C_A + K_{11}C_A C_W + K_{12}C_A C_W^2 + 2K_{21}C_A^2 C_W$$

and

$$\Delta f_W = K_{11}C_A C_W + K_{21}C_A^2 C_W + 2K_{12}C_A C_W^2$$

where f_A , Δf_W and C_W are measured quantities.

The least squares method employed for curve fitting the hydration data is similar to that used for the vapor pressure lowering data discussed earlier. In the present application we have the following situation;

$$f_A = f(C_A, C_W; K_{ij}) \quad (3-8)$$

and

$$\Delta f_W = f(C_A, C_W; K_{ij}) \quad (3-9)$$

where C_A and K_{ij} are unknown. Generally, f_A is known more accurately than Δf_W . Therefore, a proper analysis would place all the error in the bound water. Furthermore, if a set of equilibrium constants, K_{ij} , are chosen and C_A eliminated between equations (3-8) and (3-9), it would be seen that Δf_W is not a linear function of the K_{ij} . Consequently, we are faced with a non-linear least squares analysis problem involving at least three adjustable parameters.

The computational procedure followed is outlined below. After a set of K_{ij} had been estimated graphically, they were used to calculate C_A point by point from equation (3-8). These values of C_A and the same set of constants were used to calculate the concentration of bound water, $\Delta f_W(\text{calc.})$, in the same manner. For each datum a term in the following sum was obtained.

$$E = \sum_i^n \left[\Delta f_{W_i} - \Delta f_{W_i}(\text{calc.}) \right]^2$$

where n is the number of data for the system in question (about 60). The purpose of a least squares method is, of course, to minimize the sum of the residual errors, E . The minimization of E for a linear case is straightforward. However, for the non-linear case a search method is needed to find the minimum in the error surface. The search technique employed in the present problem was similar to the "Partan" method as described by Wilde.⁸²

Silén⁸¹ and Christian⁸³ have shown that the error contour associated with two adjustable parameters is an elliptical paraboloid in the

vicinity of the minimum; that is, a contour which is parabolic in any vertical cross-section and elliptical in any horizontal cross-section. Therefore, the digital computer method used to find the minimum in the error surface associated with 2 parameters utilized the fact that a vertical parabola can be estimated from any three points in space. By holding one of the two parameters constant while varying the other a vertical cross-section of the surface is obtained. Since this cross-section is parabolic, errors were obtained from three closely spaced values of the variable parameter. From these three error values the location of the minimum in the parabola was estimated. Then new errors were found for three points about this new value of the parameter and another minimum estimated. Repetition of this procedure continued until the values of the parameter at the estimated minima agreed within 0.2 percent.

Next the second parameter is incremented by a small value and the entire procedure is repeated to find the minimum in this new vertical cross-section parallel to the first. The line of steepest descent toward the absolute minimum is taken as that connecting these two minima. Further searching for the overall minimum is then confined to this line. To insure that the absolute minimum found from the first try was indeed the true minimum in the error surface, the entire procedure was repeated using the values of the parameters at the first overall minimum. Generally the second minimum was not found to differ drastically from the

first. The values of the adjustable parameters at the final minimum are the least squares values.

In addition to the best value of the equilibrium constants, the errors in the parameters are also needed. For example, a constant with an error of its own magnitude probably would not reflect a very important species in solution. Therefore, after the final minimum has been found the relation of Christian⁷⁸

$$\Delta\text{RMSD} = \frac{\text{RMSD}(\text{min})}{2(n - p)}$$

is used to effectively make a horizontal cross-section through the error contour at a height of ΔRMSD above the absolute minimum. From the ellipse thus defined, it was possible to find the parameters of the relation

$$\Delta\text{RMSD} = A\Delta x^2 + B\Delta y^2 + C\Delta x\Delta y \quad (3-10)$$

where the origin of the coordinate system has been arbitrarily taken as the center of the ellipse and where x and y refer to the equilibrium constants in question, from six values of the adjustable parameters; that is, x and y , x and y separately incremented and decremented, and from x and y incremented simultaneously. Once A , B and C have been obtained Δx and Δy could be calculated from equation (3-10). It has been shown⁸³ that Δx and Δy obtained from the points of contact of the vertical and horizontal tangents to the standard error ellipse represent one- σ value in these equilibrium constants.

Three-parameter fits were obtained using the same program and varying the third equilibrium constant "manually." It was then possible to calculate the absolute minimum from three error values near the absolute minimum associated with these fits. One- σ values of the error in the third parameter were obtained graphically. Interestingly, it was found from the three-parameter fits that near the final minimum the equilibrium constants were linearly related to a close approximation.

All the two- and three-parameter fits tried on the hydration data in the three solvents are offered for comparison in Tables XXVI through XXIII. It is immediately apparent that two parameters are not sufficient to adequately fit the data in any of the systems. Furthermore, only three of the three-parameter fits (K_{20} is not considered a parameter here since it was determined independently), where all the constants remain positive, would appear to be at all reasonable; these are AW , A_2W , A_2W_2 and AW , AW_2 , A_2W for the carbon tetrachloride and benzene systems and AW , AW_2 , A_2W and AW , AW_2 , A_2W_2 for the DCE systems. The reasons for choosing a particular set over the other will be deferred until the next sections. However, the measured values for the hydration studies along with the calculated Δf_w and C_A values for the chosen parameters are given in Tables XIX through XXV.

TABLE VII

VAPOR PRESSURE LOWERING OF CARBON TETRACHLORIDE
BY DIPHENYLMETHANE 25°C

Initially	158.1832 g of CCl_4 2.4766 g of DPM	$P_{\text{CCl}_4}^0 = 114.08 \text{ Torr}$ M. W. DPM = 168.23 g/mole
	$X_2 = 0.01414$	

g CCl_4 removed	X_2	Pobs. (Torr)	Δp	Apparent Molecular Weight
42.5934	0.01921	111.95	2.13	174.0
		111.96	2.12	174.9
		111.92	2.16	171.6
12.1882	0.02143	111.61	2.47	167.1
		111.66	2.41	170.6
		111.60	2.47	166.5
13.0308	0.02445	111.25	2.83	166.4
		111.20	2.88	163.4
13.5436	0.02863	110.82	3.26	169.2
		110.80	3.28	168.1
		110.82	3.26	169.2
12.1953	0.03383	110.09	3.99	163.0
		110.02	4.06	159.9
		110.03	4.05	160.6

93.5523 g Total

Avg. 167.3

weight of final solution 62.9046

weight of DPM - 2.4766

60.4280 g CCl_4 initial weight - final weight = 64.6309 g CCl_4

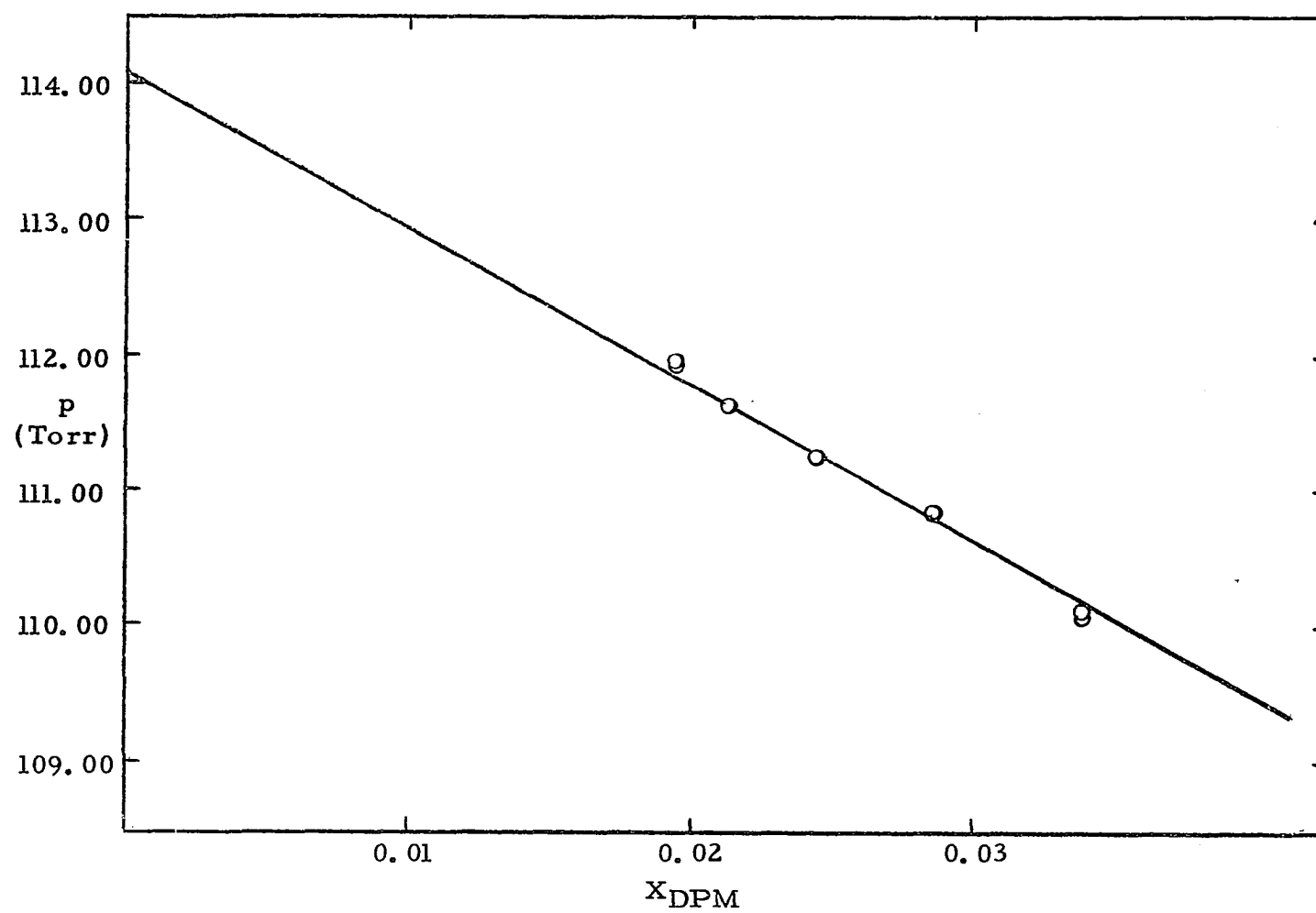


Figure IV. Vapor Pressure Lowering of Carbon Tetrachloride by Diphenylmethane 25°C

TABLE VIII

VAPOR PRESSURE LOWERING OF CARBON TETRACHLORIDE
BY N-METHYL-2-PYRROLIDONE 25°C

Run I

Initially	94.3586 g of CCl_4 0.4894 g of NMP	$p^\circ \text{CCl}_4 = 114.08 \text{ Torr}$ $p^\circ \text{CCl}_4(\text{calc.}) = 114.05 \text{ Torr}$ $X_2 = 0.007985$		
g CCl_4 removed	X_2	$P_{\text{obs.}}(\text{Torr})$	$P_{\text{calc.}}(\text{Torr})$	Δp
28.5076	0.01119	112.79 112.80 112.76	112.83	1.29 1.28 1.32
7.9734	0.01264	112.67 112.64 112.62	112.68	1.41 1.44 1.46
11.2934	0.01555	112.42 112.39 112.37	112.39	1.66 1.69 1.71
9.9567	0.01956	112.00 111.99 112.01	111.99	2.08 2.09 2.07
10.8067	0.02723	111.32 111.31 111.30	111.26	2.76 2.77 2.78

68.5378 g Total

TABLE VIII--Continued

Run II

Initially	158.003 g of CCl_4 0.7106 g of NMP	$p_{\text{CCl}_4}^{\circ} = 114.08 \text{ Torr}$ $p_{\text{CCl}_4}^{\circ} (\text{calc.}) = 114.05 \text{ Torr}$		
	$X_2 = 0.006836$			
g CCl_4 removed	X_2	$p_{\text{obs.}} (\text{Torr})$	$p_{\text{calc.}} (\text{Torr})$	Δp
65.3675	0.01177	112.86 112.88	112.77	1.22 1.20
11.3474	0.01339	112.65 112.53 112.61	112.60	1.43 1.55 1.47
20.0093	0.01768	112.22 112.20	112.18	1.86 1.88
13.1137	0.02240	111.77 111.74 111.81	111.68	2.31 2.34 2.27

109.8379 g Total

Finally weight of solution in the flask 48.472
weight of NMP - 0.711

48.761 g of CCl_4
remaining

initial weight of CCl_4 158.003
weight of CCl_4 removed - 109.838

49.163 g of CCl_4
remaining
(calculated)

TABLE VIII--Continued

Run III

Initially	157.8990 g of CCl_4 2.1341 g of NMP	$p_{\text{CCl}_4}^0 = 114.08 \text{ Torr}$ $p_{\text{CCl}_4}^0 (\text{calc.}) = 114.05 \text{ Torr}$		
	$X_2 = 0.02054$			
g CCl_4 removed	X_2	$p_{\text{obs.}} (\text{Torr})$	$p_{\text{calc.}} (\text{Torr})$	Δp
40.9886*	0.02706*	111.36 111.38	111.28	2.72 2.70
10.9779	0.02973	110.90 110.86	111.03	3.19 3.22
14.3361	0.03412	110.50 110.46	110.62	3.58 3.62
11.4470	0.03868	110.11 110.14	110.21	3.97 3.94
11.2096	0.04451	109.70 109.65	109.69	4.38 4.43
14.9174	0.05560 [†]	108.78 108.76 108.81	108.71	5.30 5.32 5.27

weight of final solution 56.2565
weight of NMP - 2.1341
54.1224

*Obtained by difference from final weight and initial weight when the trap broke.

[†]Not shown on the corresponding graph.

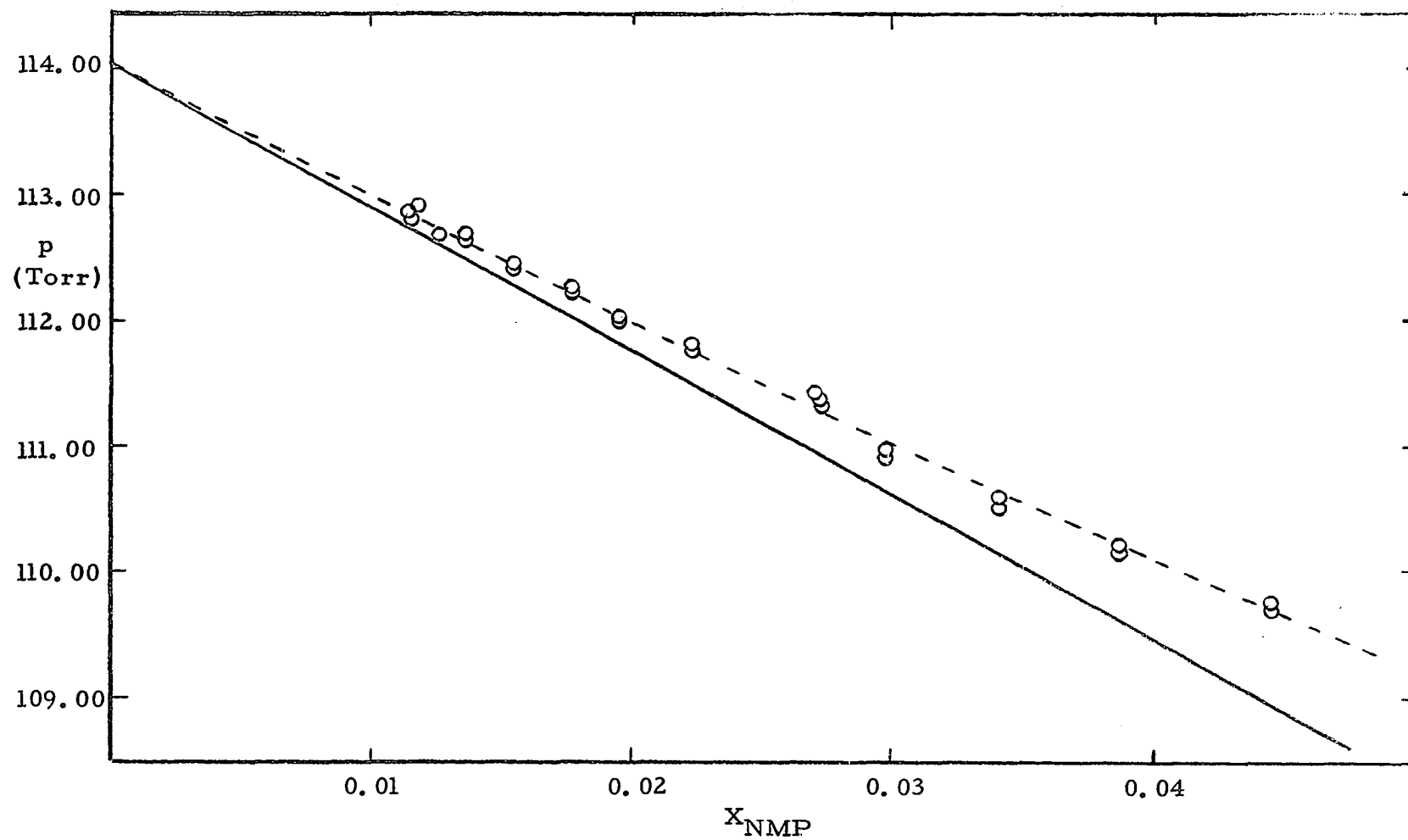


Figure V. Vapor Pressure Lowering of Carbon Tetrachloride by N-Methyl-2-Pyrrolidone 25°C

TABLE IX

VAPOR PRESSURE LOWERING OF BENZENE
BY DIPHENYLMETHANE 25°C

Run I

Initially	87.0428 g of Benzene 3.0025 g of DPM $X_2 = 0.01576$	$p^o = 95.06$ Torr M. W. DPM = 168.23 g/mole		
g of Benzene removed	X_2	$p_{\text{obs.}}$ (Torr)	p	Apparent Molecular Weight
18.2409	0.01986	93.17	1.89	168.0
		93.21	1.85	171.7
		93.15	1.91	166.2
5.6929	0.02161	92.92	2.14	161.3
		92.96	2.10	164.5
		93.02	2.04	169.4
		92.99	2.07	166.9
7.4892	0.02445	92.68	2.38	164.2
		92.72	2.34	167.1
		92.71	2.35	166.3
11.1773 [†]	0.03041	92.20	2.86	170.1
		92.23	2.83	172.0
		92.20	2.86	170.1
8.2434	0.03708	91.54	3.52	168.5
		91.59	3.47	171.0
		91.55	3.51	169.0

50.8438 g Total

weight of final solution 39.2015 g

weight of DMP - 3.0025

36.1990 g of Benzene

[†] Some lost - corrected by difference in final and initial weights.

TABLE IX--Continued

Run II

Initially	87.0297 g of Benzene 4.3517 g of DPM $X_2 = 0.02268$	$p^0 = 95.06$ Torr M. W. $DPM = 168.23$ g/mole		
g of Benzene removed	X_2	$P_{obs.}$ (Torr)	Δp	Apparent Molecular Weight
16.4044	0.02781	92.46	2.60	171.1
		92.49	2.57	173.2
		92.47	2.59	171.8
6.7621	0.03068	92.21	2.85	174.1
		92.23	2.83	172.2
		92.21	2.85	174.1
7.2747	0.03447	91.77	3.27	167.5
		91.77	3.29	167.5
		91.78	3.28	168.1
5.3878	0.03796	91.40	3.66	166.2
		91.38	3.68	164.8
		91.43	3.63	167.2
6.6897	0.04342	90.95	4.11	169.0
		90.92	4.14	167.7
		90.93	4.13	168.1
4.1537	0.04768	90.52	4.54	167.9
		90.50	4.56	167.2
		90.50	4.56	167.2
5.2619	0.05444	90.04	5.02	173.7
		90.02	5.04	173.0
		90.04	5.02	173.7

51.9343

weight of final solution 39.3006

weight of DPM - 4.3517

34.9489 g of Benzene

Initial weight of Benzene - total weight removed = 35.0954 g

Average apparent molecular weight from both runs: 168.5

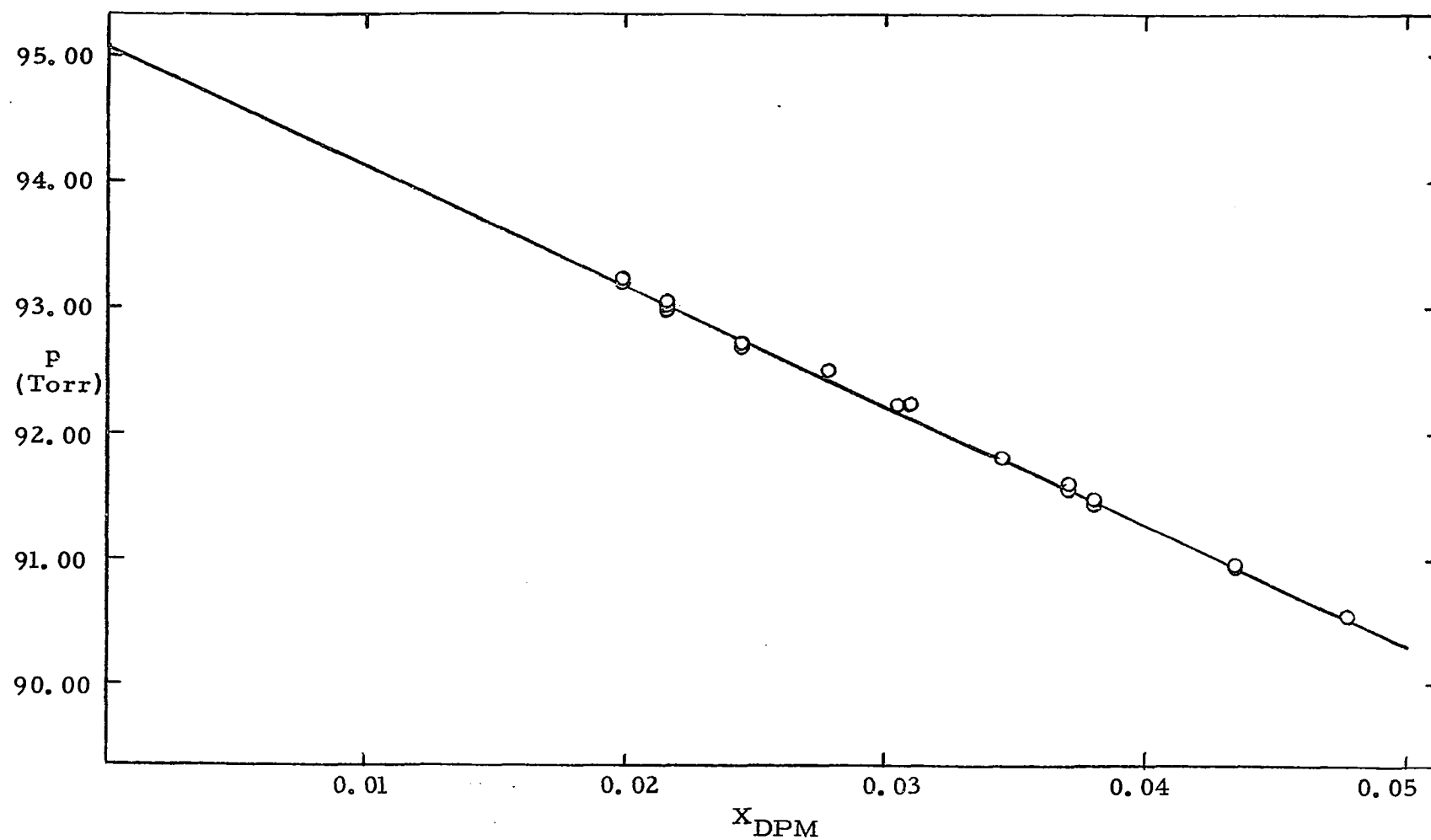


Figure VI. Vapor Pressure Lowering of Benzene by Diphenylmethane 25°C

TABLE X

VAPOR PRESSURE LOWERING OF BENZENE
BY N-METHYL-2-PYRROLIDONE 25°C

Run I

Initially	87.0675 g of Benzene 1.1760 g of NMP	$p^0 = 95.06$ Torr		
	$X_2 = 0.01053$	$p^0(\text{calc.}) = 95.13$ Torr		
g of Benzene removed	X_2	$p_{\text{obs.}}$ (Torr)	$p_{\text{calc.}}$ (Torr)	Δp
24.6840	0.01464	93.80	93.79	1.26
		93.81		1.25
		93.82		1.24
8.1937	0.01681	93.65	93.60	1.41
		93.60		1.46
		93.62		1.44
6.3784	0.01901	93.46	93.42	1.60
		93.45		1.61
		93.47		1.59
6.8601	0.02213	93.22	93.15	1.84
		93.22		1.84
		93.23		1.83
6.9624	0.02656	92.82	92.78	2.24
		92.83		2.23
		92.85		2.21

53.0786

weight of final solution 34.6658
weight of NMP - 1.1760
33.4898 g

Initial weight of Benzene - weight of Benzene removed = 33.9889 g

TABLE X--Continued

Run II

Initially	87.0965 g of Benzene 2.3497 g of NMP $X_2 = 0.02082$	$\langle p^0 \rangle = 95.06$ Torr $p^0(\text{calc.}) = 95.13$ Torr		
g of Benzene removed	X_2	$p_{\text{obs.}}$ (Torr)	$p_{\text{calc.}}$ (Torr)	Δp
15.7474	0.02529	93.02		2.04
		93.02	.92.89	2.04
		93.03		2.03
5.5883	0.02738	92.75		2.31
		92.73	.92.72	2.33
		92.71		2.35
6.5822	0.03034	92.48		2.58
		92.45	92.47	2.61
		92.50		2.56
8.5214	0.03526	92.04		3.02
		92.01	92.08	3.05
		92.04		3.02
6.9778	0.04067	91.53		3.53
		91.62	91.64	3.44
		91.61		3.45
8.0434	0.04935	91.62		3.44
		90.92		4.15
		90.92	90.96	4.14
		90.92		4.14

50.7505

weight of final solution 39.4084
weight of NMP - 2.3497
37.0587 g

Weight of initial Benzene - weight of Benzene removed = 36.3460 g

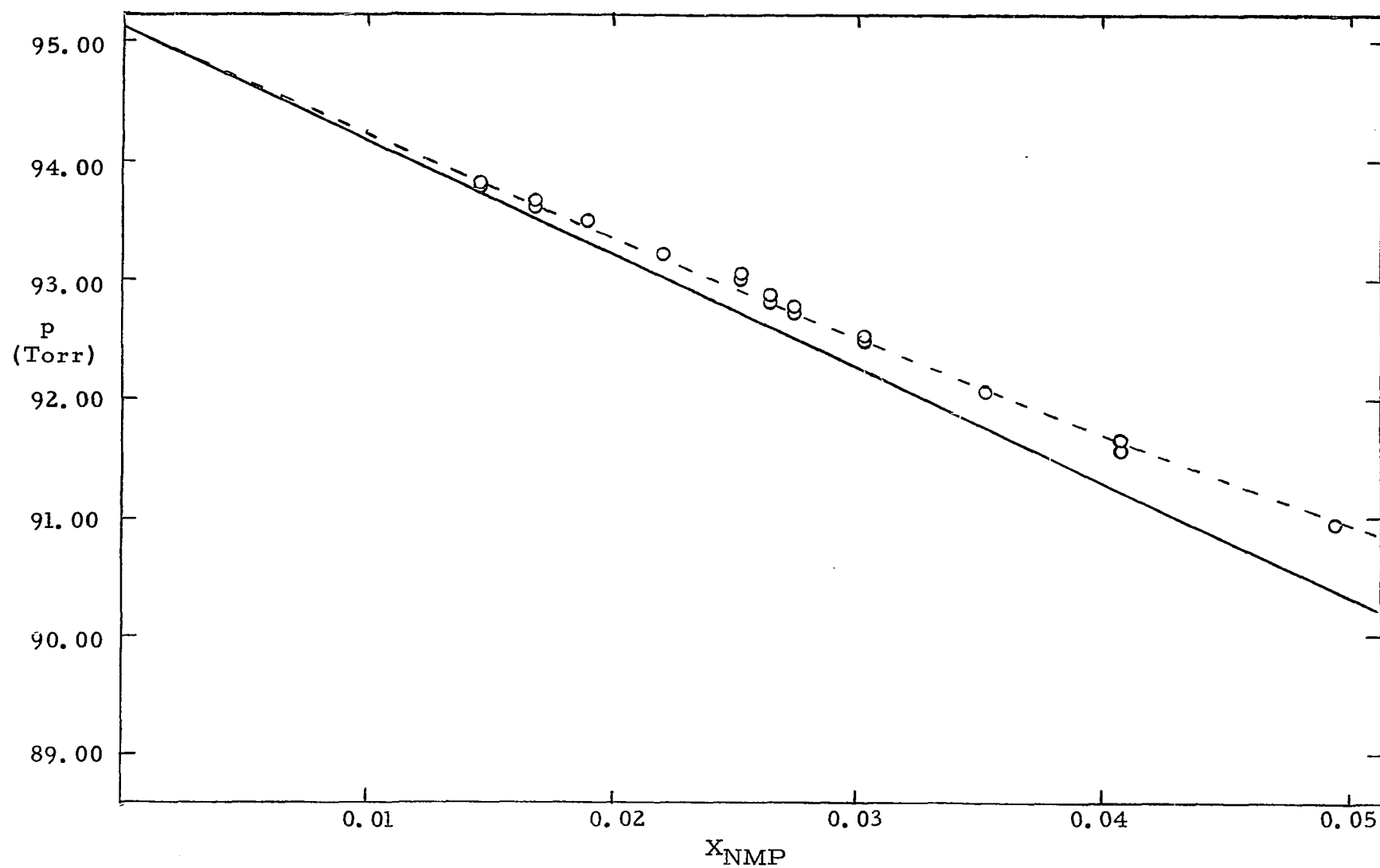


Figure VII. Vapor Pressure Lowering of Benzene by N-Methyl-2-Pyrrolidone 25°C

TABLE XI

SOLUBILITY OF WATER IN CARBON TETRACHLORIDE
AT SEVERAL ACTIVITIES 25°C

a_W	C_W (moles/liter)	C_W calc.
		(using $C_W^o = 0.0087$)
0.400	0.00349	0.00348
	0.00376	
0.550	0.00451	0.00478
	0.00486	
0.700	0.00587	0.00609
	0.00619	

TABLE XII

SOLUBILITY OF WATER IN CARBON TETRACHLORIDE
AT SEVERAL ACTIVITIES 15°C

a_W	C_W (moles/liter)	C_W calc.
0.400	0.00242	0.00229
	0.00229	
	0.00226	
0.550	0.00304	0.00315
	0.00306	
	0.00308	
0.700	0.00374	0.00401
	0.00393	
	0.00384	
1.00	0.00574	0.00573
	0.00584	
	0.00589	
	0.00573*	
	0.00588	

*Separate run.

TABLE XIII

THE SOLUBILITY OF WATER IN 1, 2-DICHLOROETHANE
AT VARIOUS WATER ACTIVITIES 25°C

$$\begin{aligned} \text{Fit to } f_W^o &= C_W^o a_W + 3K_3(C_W^o a_W)^3 \\ &= 0.110 a_W + 0.0200 a_W^3 \end{aligned}$$

f_W^o (mole/liter)	a_W	f_W^o (calc.)
0.0279	0.250	0.0278
0.0284		
0.0284		
0.0458	0.402	0.0455
0.0459		
0.0457		
0.0602	0.529	0.0612
0.0595		
0.0600		
0.0600		
0.0818	0.695	0.0831
0.0822		
0.0828		
0.1335	1.00	0.1300
0.1321		
0.1319		
0.1284		
0.1296		
0.1291		

TABLE XIV

THE SOLUBILITY OF WATER IN 1, 2-DICHLOROETHANE
AT VARIOUS WATER ACTIVITIES 15°C

$$\text{Fit to } f_W^o = C_W^o a_W + 3K_3(C_W^o a_W)^3$$

$$= 0.080 a_W + 0.01843 a_W^3$$

f_W^o (mole/liter)	a_W	f_W^o (calc.)
0.0206	0.250	0.0203
0.0201		
0.0201		
0.0338	0.402	0.0334
0.0342		
0.0340		
0.0462	0.529	0.0450
0.0458		
0.0461		
0.0663	0.695	0.0618
0.0651		
0.0648		
0.0929	1.00	0.0984
0.0928		
0.0932		
0.0937		
0.0931		
0.0969		
0.0980		
0.0969		

TABLE XV

SOLUBILITY OF WATER IN BENZENE
AT SEVERAL ACTIVITIES 15°C

a_W	f_W^0 (moles/liter)	f_W^0 calc. (assuming dimers)	f_W^0 calc. (assuming trimers)
0.250	0.00612	0.00577	0.00589
	0.00597		
	0.00592		
	0.00614		
	0.00605		
0.402	0.00613	0.00952	0.00958
	0.00936		
	0.00934		
	0.00942		
	0.00931		
0.529	0.00935	0.01277	0.01276
	0.00935		
	0.01266		
	0.01247		
	0.01271		
0.695	0.01265	0.01722	0.01713
	0.01268		
	0.01735		
	0.01730		
	0.01673		
0.850	0.01703	0.02155	0.02147
	0.01688		
	0.02245		
	0.02233		
0.953	0.02180	0.02453	0.02452
	0.02151		
	0.02460		
	0.02442		
	0.02460		

TABLE XV--Continued

a_w	f_w^o (moles/liter)	f_w^o calc. (assuming dimers)	f_w^o calc. (assuming trimers)
	0.02601		
	0.02601		
	0.02605		
1.00	0.02553	0.02592	0.02597
	0.02553		
	0.02566		
	0.02582		
	0.02586		

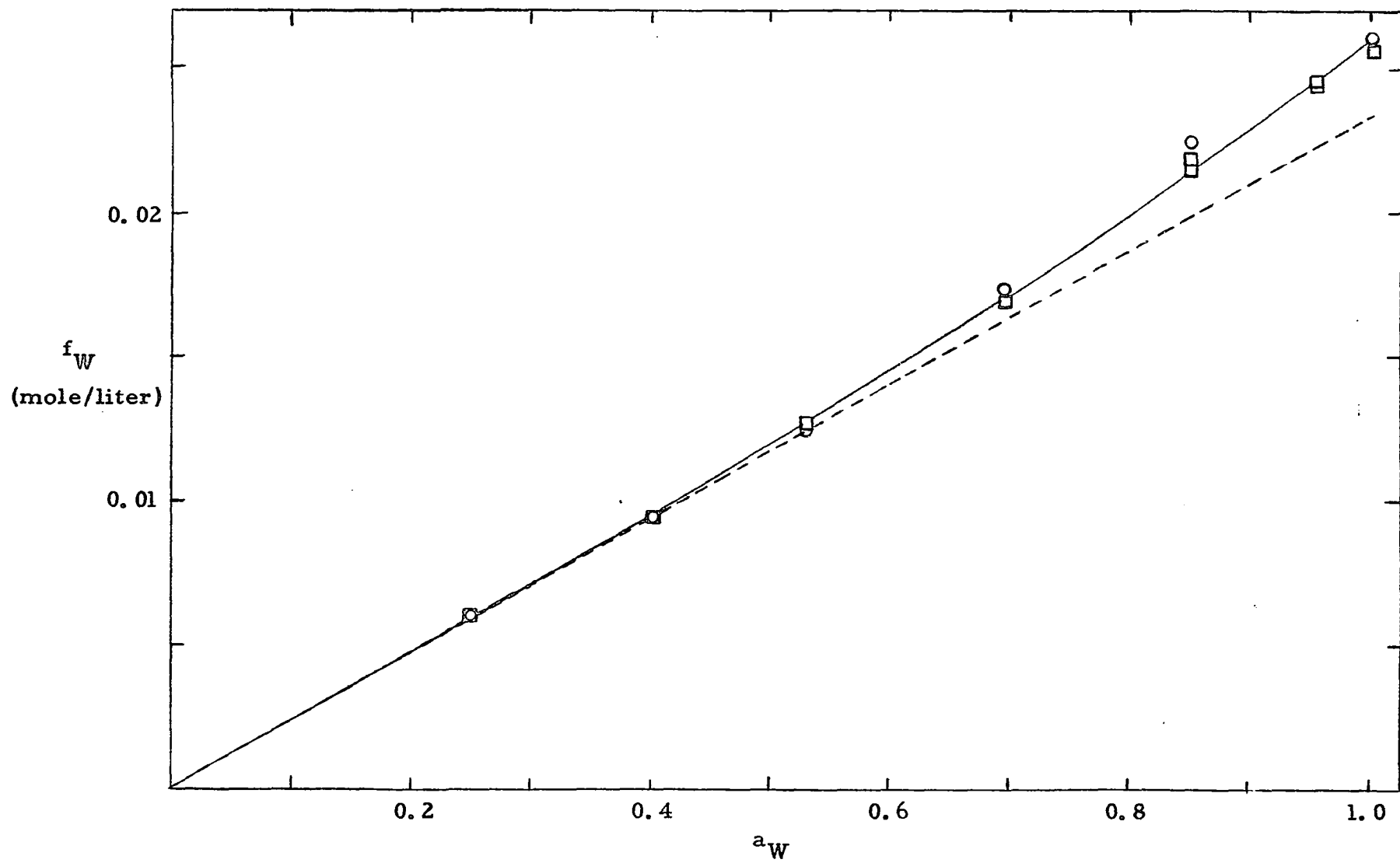


Figure VIII. Solubility of Water in Benzene as a Function of Water Activity 15°C

TABLE XVI

COMPARISON OF LEAST SQUARES FITS
FOR WATER IN BENZENE 15°C

Fit to $f_W^o = C_W^o a_W + mK_m(C_W^o a_W)^m + nK_n(C_W^o a_W)^n$				
Species	RMSD x 10 ⁴	$C_W^o \frac{\text{mole}}{\text{liter}}$	K_m	K_n
Monomer m = n = 0	6.060	0.02535	0	0
Monomer-dimer m = 2; n = 0	2.958	0.02216	3.82	0
Monomer-trimer m = 3; n = 0	3.043	0.02340	6.66	0
Monomer-tetramer m = 4; n = 0	3.296	0.02386	16.43	0
Monomer-dimer-trimer m = 2; n = 3	3.002	0.02221	3.61	35.7
Monomer-dimer-tetramer m = 2; n = 4	3.000	0.02195	-	neg.
Monomer-trimer-tetramer m = 3; n = 4	2.871	0.02257	-	neg.
Monomer-trimer-hexamer m = 3; n = 6	2.732	0.02268	-	neg.

TABLE XVII

SOLUBILITY OF WATER IN BENZENE
AT SEVERAL ACTIVITIES 25°C

a_W	f_W^o (mole/liter)	f_W^o calc. (assuming tetramers)	f_W^o calc. (assuming trimers)
0.250	0.00834		
	0.00833		
	0.00824	0.00841	0.00831
	0.00897		
	0.00885		
	0.00897		
0.402	0.01332		
	0.01339		
	0.01337	0.01358	0.01350
	0.01379		
	0.01369		
	0.01371		
0.529	0.01761		
	0.01742		
	0.01744	0.01801	0.01798
	0.01788		
	0.01790		
	0.01801		
0.695	0.02377		
	0.02372	0.02404	0.02412
	0.02372		
0.702	0.02496		
	0.02443	0.02431	0.02438
	0.02417		
0.832	0.02978		
	0.02990	0.02937	0.02947
	0.02961		
0.851	0.03038		
	0.03043	0.03015	0.03024
	0.03033		

TABLE XVII--Continued

a_W	f_W^0 (mole/liter)	f_W^0 calc.	f_W^0 calc.
		(assuming tetramers)	(assuming trimers)
0.934	0.03401		
	0.03372	0.03363	0.03367
	0.03381		
0.953	0.03455		
	0.03436	0.03446	0.03448
	0.03421		
1.00	0.03637		
	0.03651		
	0.03642		
	0.03666	0.03656	0.03649
	0.03666		
	0.03634		
	0.03630		
	0.03621		

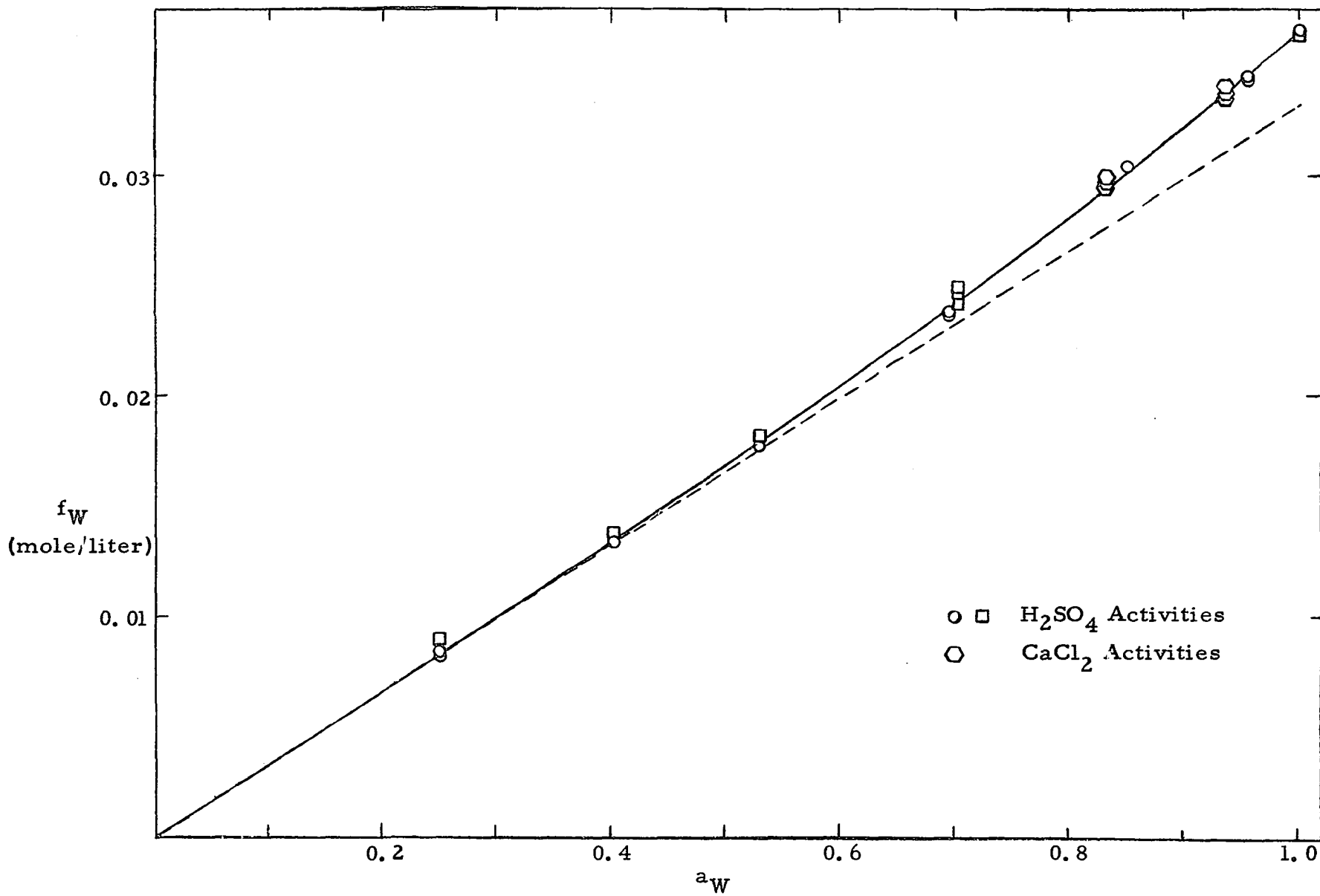


Figure IX. Solubility of Water in Benzene as a Function of Water Activity 25°C

TABLE XVIII

COMPARISON OF LEAST SQUARES FITS
FOR WATER IN BENZENE 25°C

Fit to $f_W^o = C_W^o a_W + mK_m(C_W^o a_W)^m + nK_n(C_W^o a_W)^n$				
Species	RMSD $\times 10^4$	C_W^o $\frac{\text{mole}}{\text{liter}}$	K_m	K_n
Monomer $m = n = 0$	7.519	0.03565	0	0
Monomer-dimer $m = 2; n = 0$	3.317	0.03143	2.51	0
Monomer-trimer $m = 3; n = 0$	2.999	0.03302	32.2	0
Monomer-tetramer $m = 4; n = 0$	3.054	0.03360	580	0
Monomer-dimer-trimer $m = 2; n = 3$	3.028	0.03406	neg.	neg.
Monomer-dimer-tetramer $m = 2; n = 4$	3.076	0.03313	0.490	489
Monomer-trimer-tetramer $m = 3; n = 4$	3.037	0.03318	25.0	126
Monomer-trimer-hexamer $m = 3; n = 6$	3.033	0.03296	-	neg.

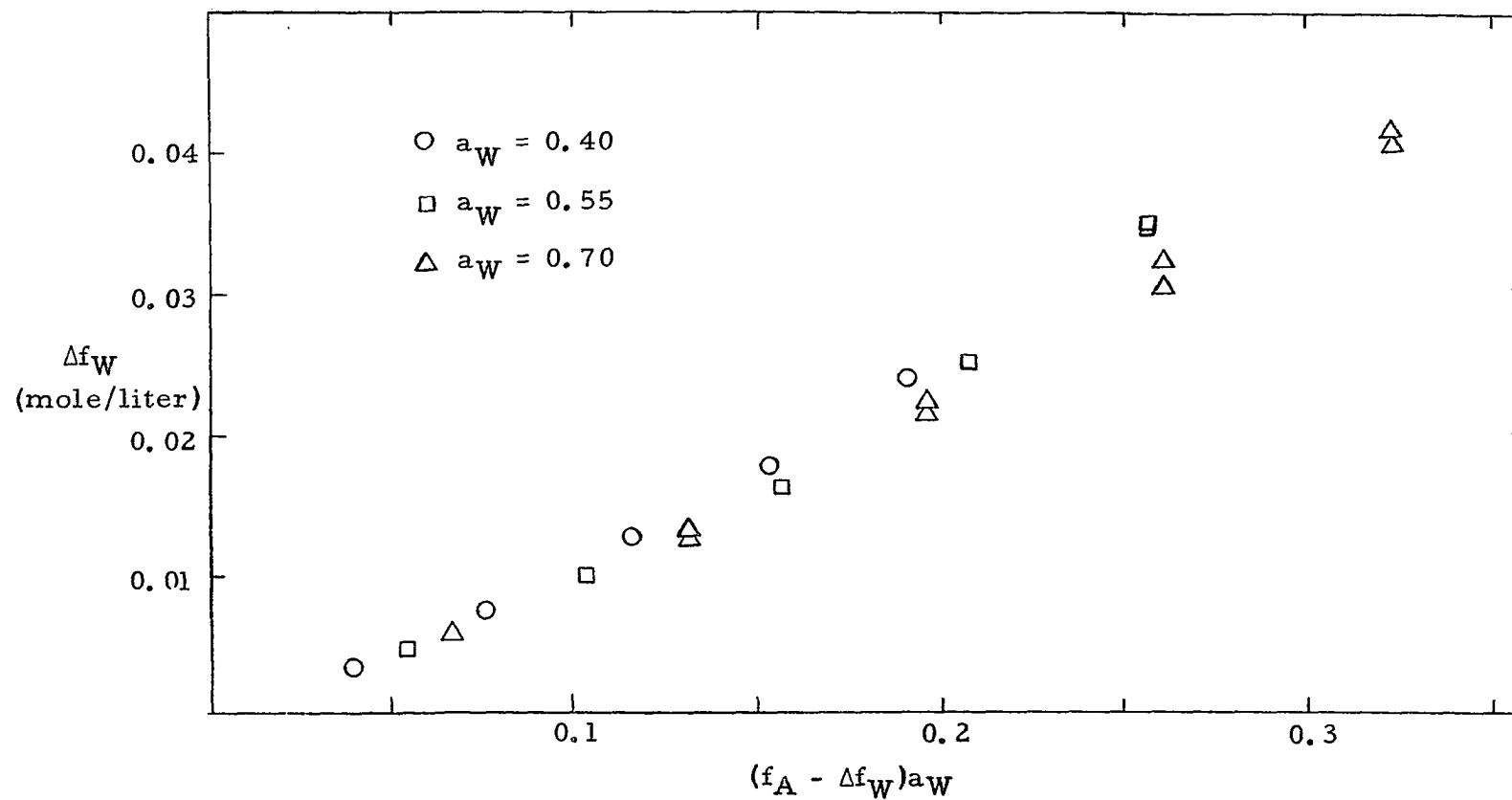


Figure X. Graphical Estimation of the Hydrated Species of N-Methyl-2-Pyrrolidone in Carbon Tetrachloride 15°C

TABLE XIX

THE HYDRATION OF N-METHYL-2-PYRROLIDONE
IN CARBON TETRACHLORIDE 25°C

Fit with $\Delta f_W = 0.079876C_A a_W + 0.33922C_A^2 a_W + 2(0.10056)C_A^2 a_W^2$				
$f_A \frac{\text{mole}}{\text{liter}}$	a_W	$\Delta f_W \frac{\text{mole}}{\text{liter}}$	$\Delta f_W(\text{calc.})$	$C_A(\text{calc.})$
0.1030	0.400	0.00390 0.00402	0.00406	0.0872
0.1961		0.00880 0.00878	0.00871	0.1517
0.2971		0.01398 0.01426	0.01438	0.2126
0.4001		0.02100 0.02041	0.02062	0.2680
0.4520	0.550	0.02361 0.02298 0.02448	0.02390	0.2940
0.1030		0.00591 0.00578	0.00558	0.0857
0.1961		0.01206 0.01192	0.01200	0.1487
0.2971		0.01989 0.02014	0.01984	0.2080
0.4001		0.02691 0.02709	0.02846	0.2618
0.4520		0.03474 0.03249 0.03514	0.03299	0.2870

TABLE XIX--Continued

$f_A \frac{\text{mole}}{\text{liter}}$	a_W	$\Delta f_W \frac{\text{mole}}{\text{liter}}$	$\Delta f_W(\text{calc.})$	$C_A(\text{calc.})$
0.1030	0.700	0.00815 0.00750	0.00709	0.0842
0.1961		0.01523 0.01556	0.01528	0.1457
0.2971		0.02533 0.02578	0.02528	0.2034
0.4001		0.03380 0.03408	0.03627	0.2557
0.4520		0.04278 0.04338 0.04288	0.04204	0.2802

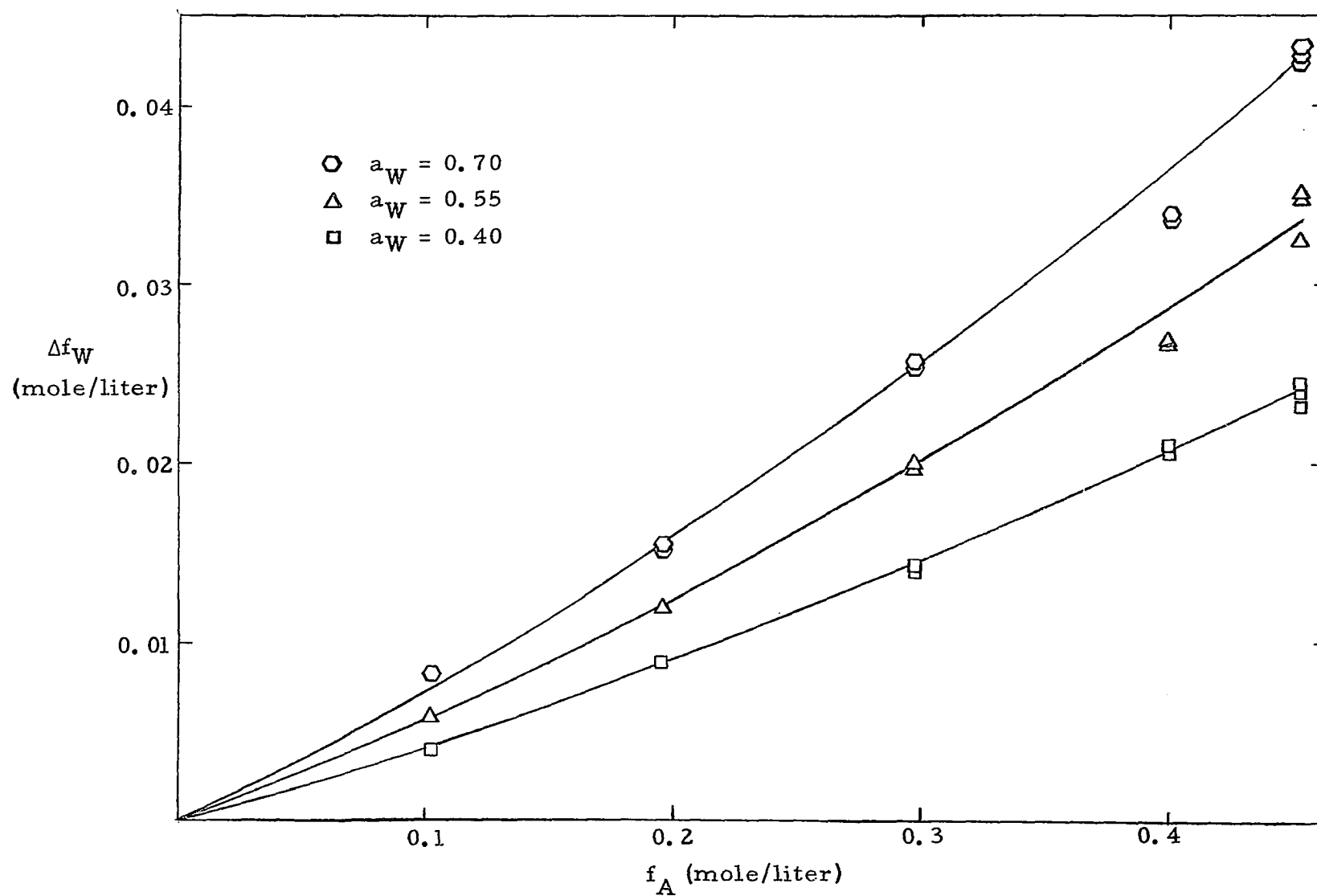


Figure XI. Solubility of Water as a Function of Water Activity and Concentration of N-Methyl-2-Pyrrolidone in Carbon Tetrachloride 25°C

TABLE XX

THE HYDRATION OF N-METHYL-2-PYRROLIDONE
IN CARBON TETRACHLORIDE 15°C

Fit with $\Delta f_W = 0.04741C_A a_W + 0.41578C_A^2 a_W + 0.07823C_A^2 a_W^2$

$f_A \frac{\text{mole}}{\text{liter}}$	a_W	$\Delta f_W \frac{\text{mole}}{\text{liter}}$	$\Delta f_W(\text{calc.})$	$C_A(\text{calc.})$
0.1042	0.400	0.00336 0.00359 0.00348	0.00313	0.0877
0.1998		0.00763 0.00757 0.00757	0.00731	0.1521
0.3018		0.01265 0.01269 0.01298	0.01255	0.2113
0.4030		0.01777 0.01782 0.01765	0.01828	0.2635
0.5014		0.02389 0.02336 0.02408	0.02422	0.3097
0.1042	0.550	0.00451 0.00439 0.00455	0.00431	0.0864
0.1998		0.00986 0.00982 0.00993	0.01005	0.1494
0.3018		0.01613 0.01644 0.01625	0.01723	0.2070
0.4030		0.02525 0.02483 0.02525	0.02506	0.2578

TABLE XX--Continued

$f_A \frac{\text{mole}}{\text{liter}}$	a_W	$\Delta f_W \frac{\text{mole}}{\text{liter}}$	$\Delta f_W(\text{calc.})$	$C_A(\text{calc.})$
0.5014		0.03467 0.03419 0.03491	0.03317	0.3026
0.1042	0.700	0.00576 0.00578	0.00549	0.0851
0.1998		0.01333 0.01261 0.01237	0.01279	0.1467
0.3018		0.02119 0.02239 0.02179	0.02187	0.2029
0.4030		0.03222 0.03300 0.03210	0.03176	0.2522
0.5014		0.04128 0.04146 0.04064	0.04198	0.2958

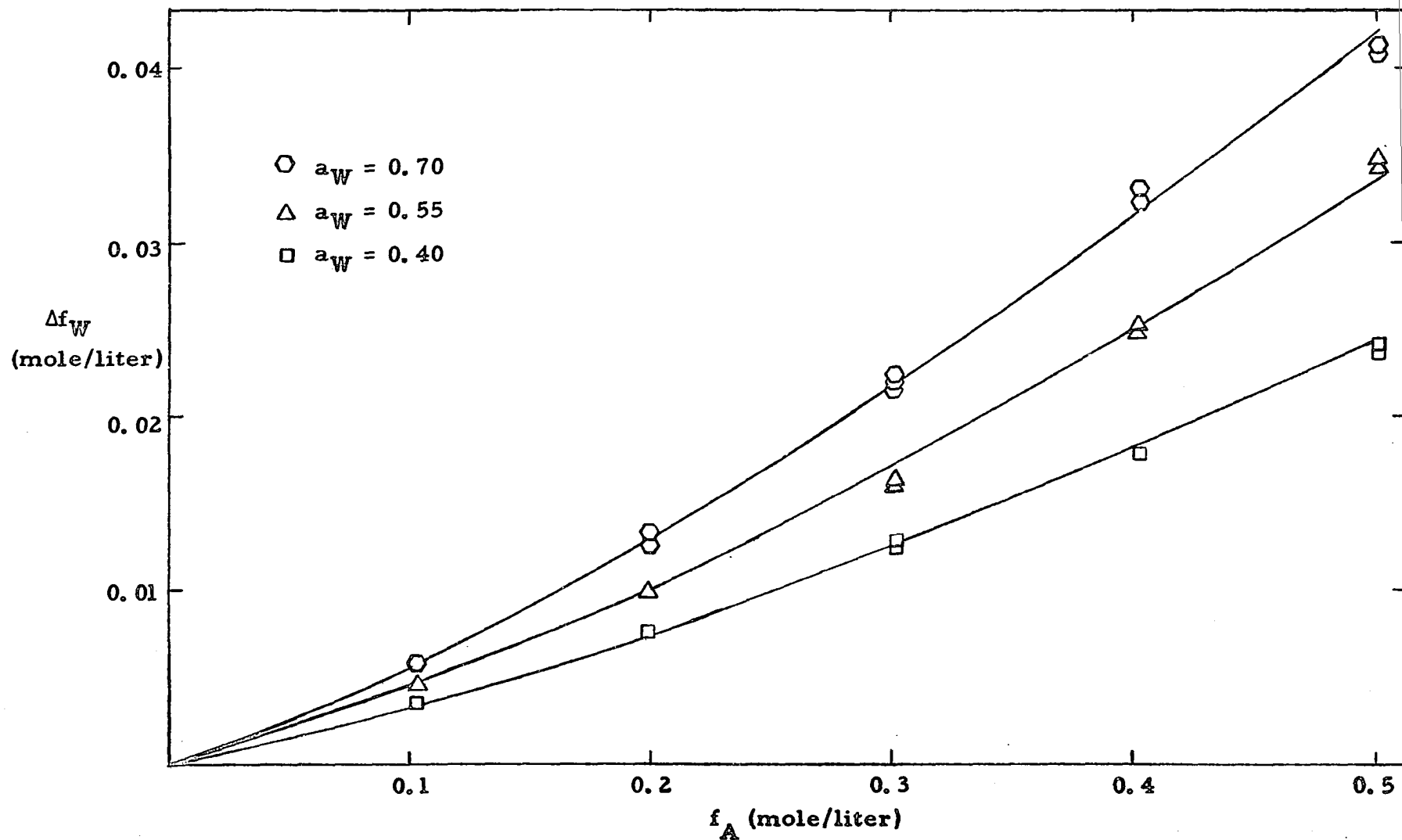


Figure XII. Solubility of Water as a Function of Water Activity and Concentration of N-Methyl-2-Pyrrolidone in Carbon Tetrachloride 15°C

TABLE XXI

THE HYDRATION OF N-METHYL-2-PYRROLIDONE
IN BENZENE 25°C

$$\text{Fit with } \Delta f_W = 0.1974 C_A a_W + 0.1426 C_A^2 a_W + 2(0.4682) C_A^2 a_W^2$$

$$\text{RMSD} = 0.852 \times 10^{-3} \text{ mole/liter}$$

$f_A \frac{\text{mole}}{\text{liter}}$	a_W	$\Delta f_W \frac{\text{mole}}{\text{liter}}$	$\Delta f_W(\text{calc.})$	$C_A(\text{calc.})$
0.1029	0.250	0.00519 0.00531	0.00526	0.0908
0.1989		0.01070 0.01072	0.01075	0.1656
0.3031		0.01705 0.01710 0.01700	0.01717	0.2389
0.4045		0.02491 0.02476 0.02472	0.02375	0.3044
0.5046	0.402	0.03143 0.03128 0.03138	0.03051	0.3646
0.1029		0.00847 0.00852	0.00858	0.0878
0.1989		0.01750 0.01745 0.01736	0.01796	0.1594
0.3031		0.02804 0.02771 0.02785	0.02918	0.2294
0.4045		0.03983 0.03954 0.03936	0.04089	0.2917

TABLE XXI--Continued

$f_A \frac{\text{mole}}{\text{liter}}$	a_W	$\Delta f_W \frac{\text{mole}}{\text{liter}}$	$\Delta f_W(\text{calc.})$	$C_A(\text{calc.})$
0.5046		0.05361 0.05313 0.05337	0.05304	0.3487
0.1029	0.529	0.01246 0.01227 0.01241	0.01135	0.0853
0.1989	.	0.02410 0.02420 0.02391	0.02413	0.1542
0.3031		0.03918 0.03930 0.03906	0.03961	0.2212
0.4045		0.05523 0.05895 0.05416 0.05464	0.05587	0.2806
0.5046		0.07249 0.07285 0.07261	0.07282	0.3349
0.1029	0.695	0.01484 0.01498	0.01495	0.0820
0.1989		0.03281 0.03305 0.03269	0.03220	0.1474
0.3031		0.05318 0.05330 0.05390	0.05330	0.2105
0.4045		0.07570 0.07642 0.07666	0.07554	0.2661
0.5046		0.09907 0.09847 0.09823	0.09877	0.3167

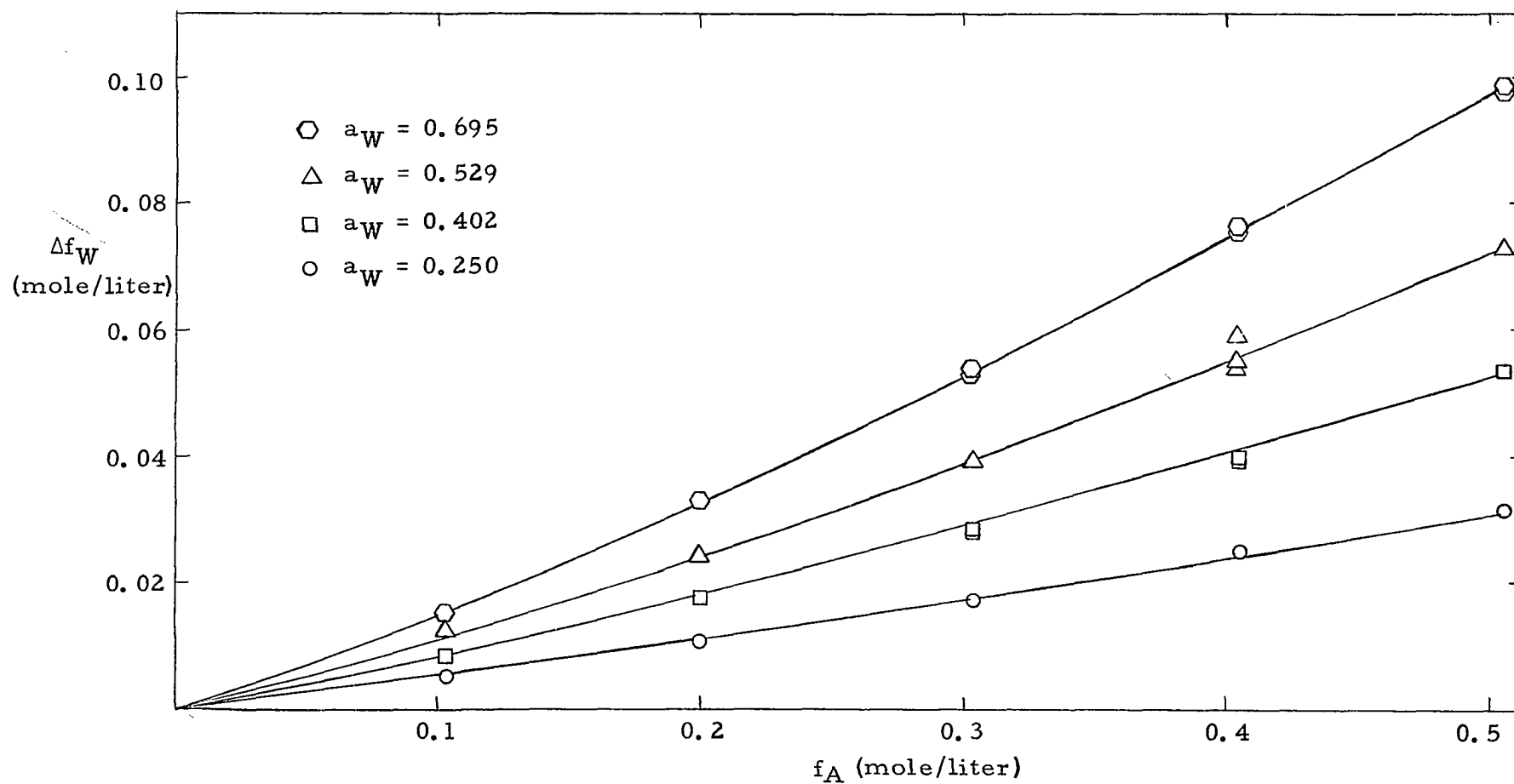


Figure XIII. Solubility of Water as a Function of Water Activity and Concentration of N-Methyl-2-Pyrrolidone in Benzene 25°C

TABLE XXII

THE HYDRATION OF N-METHYL-2-PYRROLIDONE
IN BENZENE 15°C

$$\text{Fit with } \Delta f_W = 0.1726 C_A a_W + 0.2648 C_A^2 a_W + 2(0.4154) C_A^2 a_W^2$$

$$\text{RMSD} = 1.035 \times 10^{-3} \Delta f_W$$

$f_A \frac{\text{mole}}{\text{liter}}$	a_W	$\Delta f_W \frac{\text{mole}}{\text{liter}}$	$\Delta f_W(\text{calc.})$	$C_A(\text{calc.})$
0.1028	0.250	0.00480 0.00478	0.00486	0.0903
0.2043		0.01020 0.01009	0.01054	0.1674
0.2980		0.01648 0.01628 0.01673	0.01631	0.2314
0.3978		0.02386 0.02578 0.02552 0.02586 0.02491 0.02454	0.02288	0.2938
0.4991		0.02982 0.03066 0.02944 0.02934	0.02989	0.3524
0.1028	0.402	0.00779 0.00787	0.00791	0.0874
0.2043		0.01781 0.01740 0.01785	0.01746	0.1613
0.2980		0.02709 0.02697 0.02720	0.02732	0.2223

TABLE XXII--Continued

$f_A \frac{\text{mole}}{\text{liter}}$	a_W	$\Delta f_W \frac{\text{mole}}{\text{liter}}$	$\Delta f_W(\text{calc.})$	$C_A(\text{calc.})$
0.3978		0.03824 0.03926 0.03898	0.03862	0.2815
0.4991		0.04878 0.04859 0.04907	0.05074	0.3370
0.1028	0.529	0.01036 0.01063 0.01040	0.01046	0.0850
0.2043		0.02288 0.02295 0.02329	0.02336	0.1562
0.2980		0.03541 0.03560 0.03579	0.03675	0.2146
0.3978		0.05097 0.05125 0.05059	0.05215	0.2711
0.4991		0.06944 0.06802 0.06755	0.06870	0.3240
0.1028	0.695	0.01329 0.01382 0.01374 0.01363	0.01376	0.0819
0.2043		0.03094 0.03122 0.03141	0.03105	0.1496
0.2980		0.04894 0.04922 0.04849	0.04907	0.2046

TABLE XXII--Continued

$f_A \frac{\text{mole}}{\text{liter}}$	a_W	$\Delta f_W \frac{\text{mole}}{\text{liter}}$	$\Delta f_W(\text{calc.})$	$C_A(\text{calc.})$
0.3978		0.07128 0.07033 0.07080 0.07090	0.06981	0.2577
0.4991		0.09295 0.09211 0.09277	0.09210	0.3072

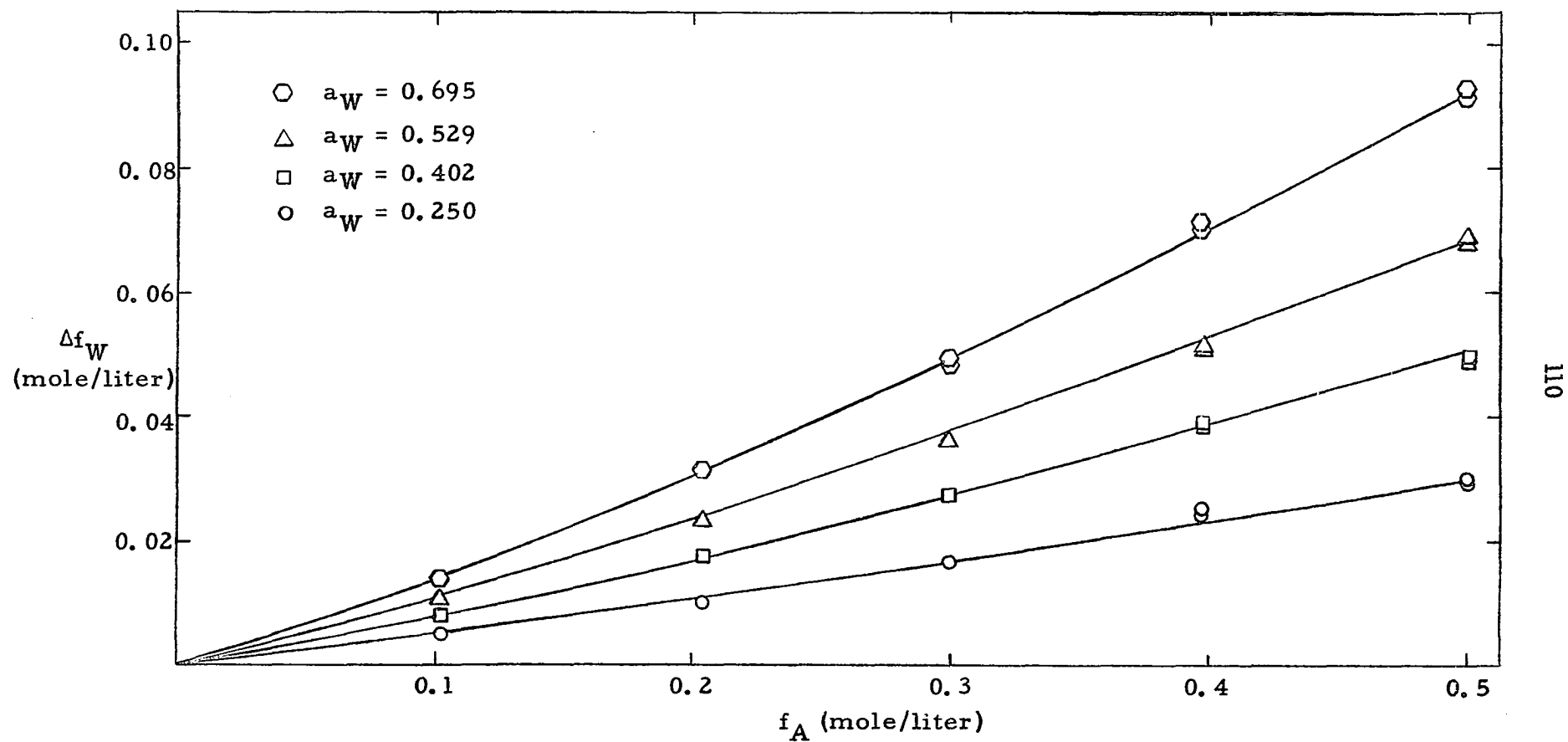


Figure XIV. Solubility of Water as a Function of Water Activity and Concentration of N-Methyl-2-Pyrrolidone in Benzene 15°C

TABLE XXIII

THE HYDRATION OF N-METHYL-2-PYRROLIDONE
IN 1, 2-DICHLOROETHANE 25°C

Fit with $\Delta f_W = 0.2628C_A a_W + 2(0.0428)C_A^2 a_W^2 + 2(0.1961)C_A^2 a_W^2$				
$f_A \frac{\text{mole}}{\text{liter}}$	a_W	$\Delta f_W \frac{\text{mole}}{\text{liter}}$	$\Delta f_W (\text{calc.})$	$C_A (\text{calc.})$
0.1015	0.250	0.0078	0.0070	0.0948
		0.0072		
		0.0076		
0.2017		0.0149	0.0142	0.1880
		0.0146		
		0.0142		
0.2997		0.0227	0.0217	0.2787
		0.0228		
		0.0230		
0.4009		0.0306	0.0298	0.3721
		0.0309		
		0.0310		
0.5080		0.0397	0.0388	0.4704
		0.0401		
		0.0395		
0.1015	0.402	0.0104	0.0114	0.0908
		0.0106		
		0.0109		
0.2017		0.0224	0.0235	0.1795
		0.0224		
		0.0221		
0.2997		0.0348	0.0362	0.2654
		0.0352		
		0.0352		
0.4009		0.0486	0.0501	0.3532
		0.0484		
		0.0485		

TABLE XXIII--Continued

$f_A \frac{\text{mole}}{\text{liter}}$	a_W	$\Delta f_W \frac{\text{mole}}{\text{liter}}$	$\Delta f_W(\text{calc.})$	$C_A(\text{calc.})$
0.5080	0.390	0.0638	0.0636	0.4473
		0.0638		
		0.0635		
0.1015	0.529	0.0152	0.0151	0.0875
		0.0149		
		0.0156		
0.2017		0.0318	0.0314	0.1724
		0.0312		
		0.0319		
0.2997		0.0474	0.0485	0.2542
		0.0484		
		0.0474		
0.4009		0.0682	0.0675	0.3375
		0.0672		
		0.0671		
0.5030		0.0884	0.0889	0.4242
		0.0894		
		0.0891		
0.1015	0.695	0.0200	0.0200	0.0833
		0.0203		
		0.0208		
0.2017		0.0411	0.0417	0.1634
		0.0419		
		0.0420		
0.2997		0.0652	0.0647	0.2400
		0.0655		
		0.0642		
0.4009		0.0912	0.0901	0.3173
		0.0906		
		0.0916		
0.5080		0.1182	0.1189	0.3973
		0.1184		
		0.1189		

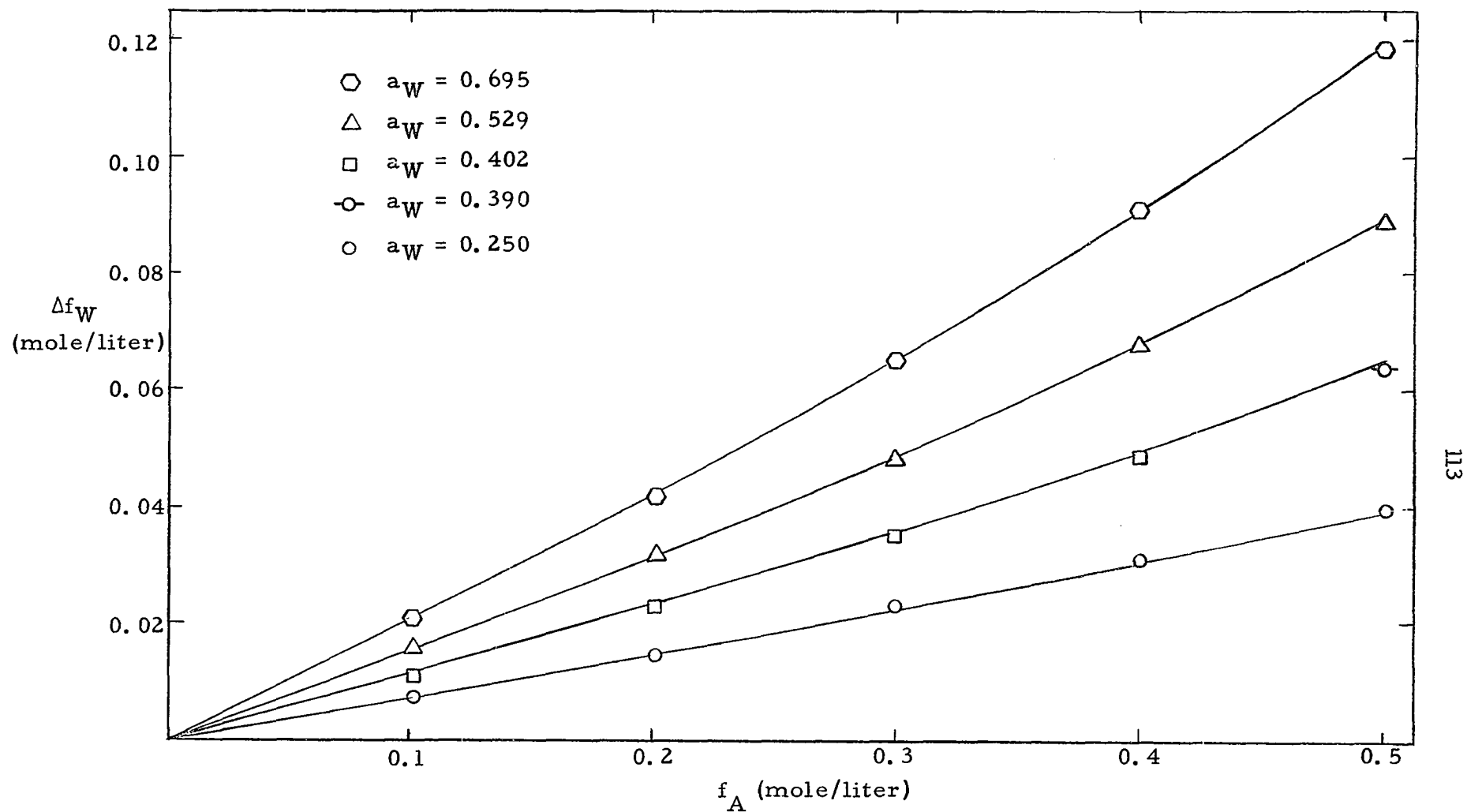


Figure XV. Solubility of Water as a Function of Water Activity and Concentration of N-Methyl-2-Pyrrolidone in 1,2-Dichloroethane 25°C

TABLE XXIV

THE HYDRATION OF N-METHYL-2-PYRROLIDONE
IN 1, 2-DICHLOROETHANE 15°C

Fit with $\Delta f_W = 0.3084C_A a_W + 2(0.0369)C_A^2 a_W^2 + 2(0.1008)C_A^2 a_W^2$				
$f_A \frac{\text{mole}}{\text{liter}}$	a_W	$\Delta f_W \frac{\text{mole}}{\text{liter}}$	$\Delta f_W(\text{calc.})$	$C_A(\text{calc.})$
0.1035	0.250	0.0060 0.0062 0.0061	0.0079	0.0958
0.2051		0.0168 0.0166 0.0168	0.0159	0.1896
0.2995		0.0237 0.0235 0.0237	0.0236	0.2766
0.4056		0.0319 0.0323 0.0313	0.0323	0.3741
0.4919		0.0426 0.0414 0.0423	0.0396	0.4533
0.1035	0.400	0.0111 0.0113 0.0108	0.0126	0.0914
0.2051		0.0252 0.0254 0.0247	0.0255	0.1807
0.2995		0.0354 0.0361 0.0357	0.0378	0.2632
0.4056		0.0507 0.0510 0.0520	0.0521	0.3556

TABLE XXIV--Continued

$f_A \frac{\text{mole}}{\text{liter}}$	a_W	$\Delta f_W \frac{\text{mole}}{\text{liter}}$	$\Delta f_W(\text{calc.})$	$C_A(\text{calc.})$
0.4919		0.0641 0.0634 0.0657	0.0641	0.4303
0.1035	0.529	0.0166 0.0159 0.0154	0.0166	0.0878
0.2051		0.0320 0.0313 0.0310	0.0336	0.1733
0.2995		0.0505 0.0506 0.0493	0.0499	0.2522
0.4056		0.0716 0.0714 0.0717	0.0690	0.3401
0.4919		0.0851 0.0841 0.0836	0.0851	0.4110
0.1035	0.695	0.0221 0.0226 0.0215	0.0217	0.0833
0.2051		0.0464 0.0466 0.0452	0.0440	0.1641
0.2995		0.0647 0.0669 0.0655	0.0656	0.2382
0.4056		0.0932 0.0908 0.0885 0.0903	0.0909	0.3205
0.4919		0.1118 0.1118 0.1118	0.1122	0.3867

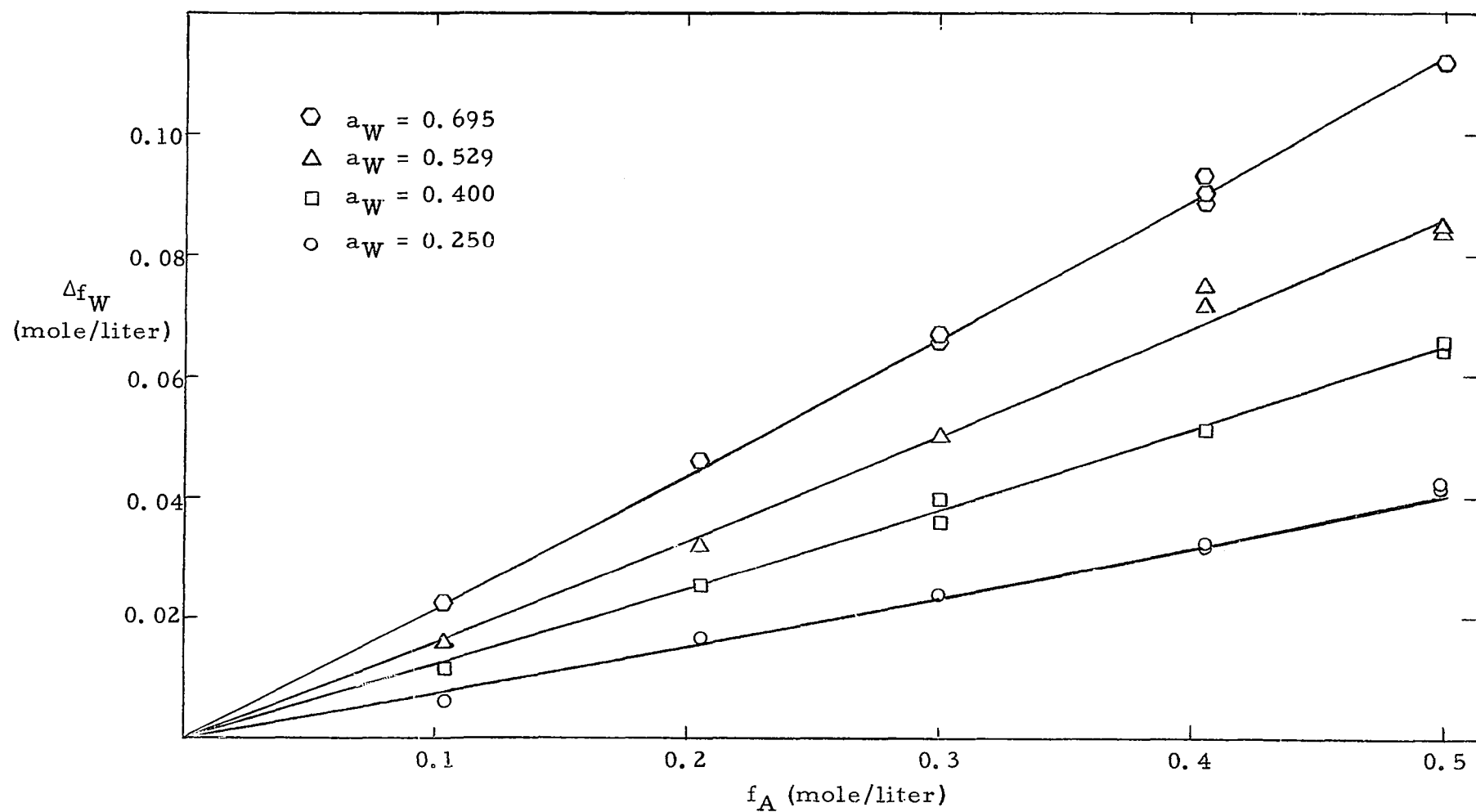


Figure XVI. Solubility of Water as a Function of Water Activity and Concentration of N-Methyl-2-Pyrrolidone in 1,2-Dichloroethane 15°C

TABLE XXV

THE HYDRATION OF N, N-DIMETHYLACETAMIDE IN
1, 2-DICHLOROETHANE 25°C

Fit with $\Delta f_W = 0.2455C_A a_W + 2(0.1034)C_A^2 a_W^2 + 2(0.1451)C_A^2 a_W^2$

$f_A \frac{\text{mole}}{\text{liter}}$	a_W	$\Delta f_W \frac{\text{mole}}{\text{liter}}$	$\Delta f_W(\text{calc.})$	$C_A(\text{calc.})$
0.0985	0.250	0.0077	0.0070	0.0921
		0.0077		
		0.0076		
0.1986		0.0153	0.0144	0.1854
		0.0159		
		0.0155		
0.2986		0.0230	0.0221	0.2783
		0.0227		
		0.0233		
0.3992		0.0321	0.0301	0.3715
		0.0324		
		0.0323		
0.4983		0.0398	0.0383	0.4630
		0.0393		
		0.0395		
0.0985	0.402	0.0114	0.0120	0.0878
		0.0116		
		0.0120		
0.1986		0.0243	0.0248	0.1767
		0.0241		
		0.0238		
0.2986		0.0372	0.0383	0.2648
		0.0370		
		0.0369		

TABLE XXV -- Continued

$f_A \frac{\text{mole}}{\text{liter}}$	a_W	$\Delta f_W \frac{\text{mole}}{\text{liter}}$	$\Delta f_W(\text{calc.})$	$C_A(\text{calc.})$
0.3992		0.0505 0.0505 0.0503	0.0524	0.3527
0.4983		0.0656 0.0665 0.0658	0.0670	0.4387
0.0985	0.529	0.0182 0.0180 0.0175	0.0164	0.0845
0.1986		0.0341 0.0349 0.0343	0.0341	0.1694
0.2986		0.0538 0.0544 0.0544	0.0527	0.2532
0.3992		0.0709 0.0715 0.0717	0.0724	0.3366
0.4983		0.0905 0.0921 0.0919	0.0926	0.4178
0.0985	0.695	0.0208 0.0212 0.0200	0.0225	0.0800
0.1986		0.0471 0.0463 0.0471	0.0468	0.1598
0.2986		0.0731 0.0726 0.0728	0.0724	0.2381

TABLE XXV--Continued

$f_A \frac{\text{mole}}{\text{liter}}$	a_W	$\Delta f_W \frac{\text{mole}}{\text{liter}}$	$\Delta f_W(\text{calc.})$	$C_A(\text{calc.})$
0.3992		0.0992	0.0993	0.3156
		0.0990		
		0.0990		
0.4983		0.1278	0.1271	0.3907
		0.1284		
		0.1296		

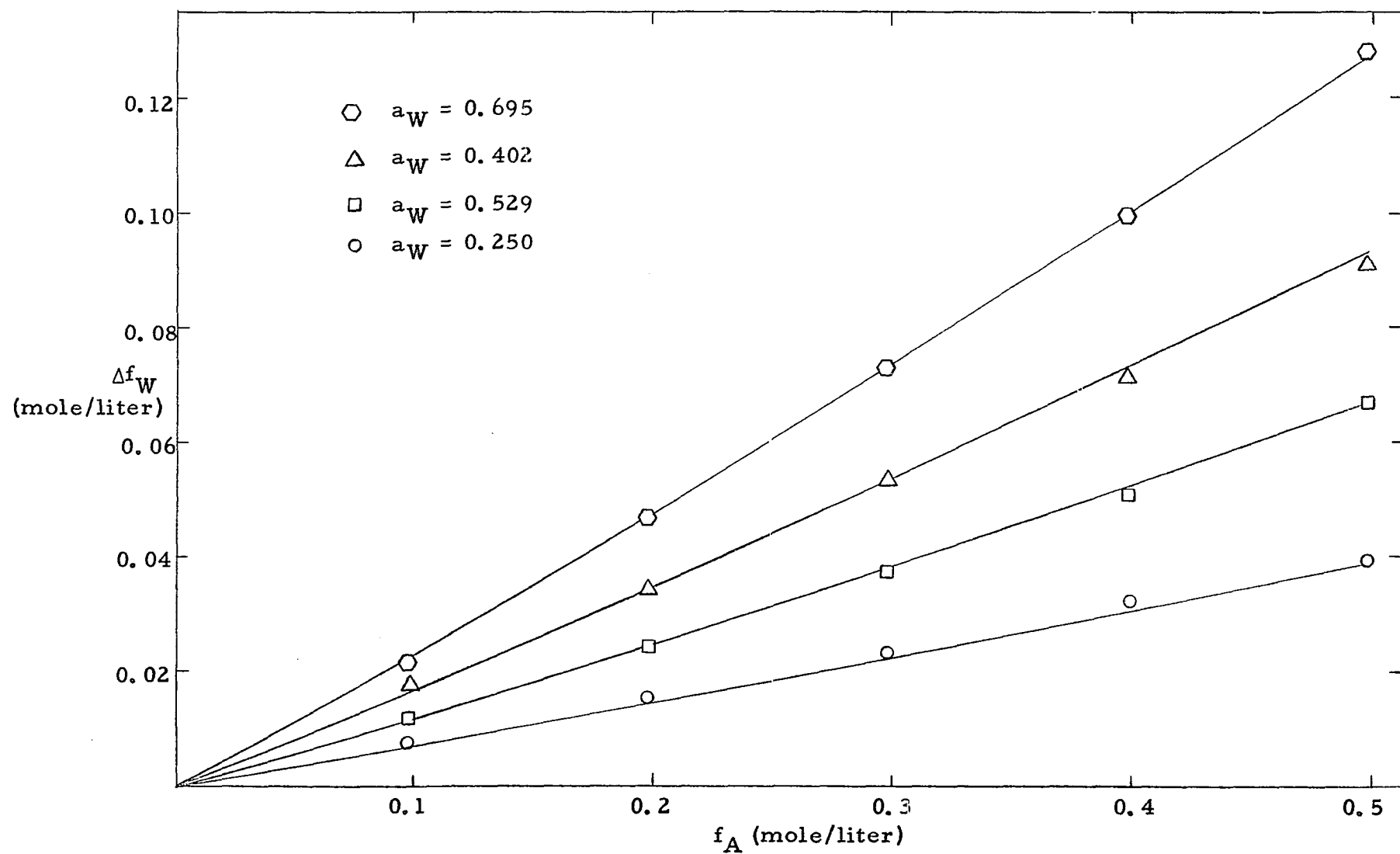


Figure XVII. Solubility of Water as a Function of Water Activity and Concentration of N, N-Dimethylacetamide in 1, 2-Dichloroethane 25°C

TABLE XXVI

COMPARISON OF THE LEAST SQUARES FITS FOR N-METHYL-
2-PYRROLIDONE IN CARBON TETRACHLORIDE

25°C

K_{20}	K_{11}	K_{12}	K_{21}	K_{22}	C_W^0	$\text{RMSD} \times 10^3$
0.708	14.13	0	0	2840	0.0087	1.805
0.708	9.19	0	39.0	1330	0.0087	0.995
0.708	18.85	-850	0	4550	0.0087	1.084
0.708	5.8	0	51	0	0.0087	1.249
0.708	5.8	316	53.8	0	0.0087	1.010
0.708	8.02	107	43.7	920	0.0087	1.012

15°C

K_{20}	K_{11}	K_{12}	K_{21}	K_{22}	C_W^0	$\text{RMSD} \times 10^3$
0.790	16.6	0	0	7690	0.00573	2.058
0.790	8.29	0	72.6	2385	0.00573	0.659
0.790	26.4	-2440	0	11680	0.00573	0.853
0.840	8.5	0	90	0	0.00573	0.881
0.840	3.2	650	93	0	0.00573	0.667
0.790	8.05	31.4	73.5	2265	0.00573	0.667

Note: All equilibrium constants are for the formation of the species from their respective monomers and are given in molar units.

TABLE XXVII

COMPARISON OF THE LEAST SQUARES FITS FOR N-METHYL-
2-PYRROLIDONE IN BENZENE

25°C

K_{20}	K_{11}	K_{12}	K_{21}	K_{22}	C_W^0	$\text{RMSD} \times 10^3$
0.394	6.67	0	0	444	0.0330	1.194
0.394	5.98	0	4.32	430	0.0330	0.852
0.394	7.17	-24.4	0	505	0.0330	0.980
0.394	8.2	0	13	0	0.0330	4.383
0.394	-0.45	150	25.6	0	0.0330	<1.1
0.394	4.48	39.6	9.45	318	0.0330	0.793

15°C

K_{20}	K_{11}	K_{12}	K_{21}	K_{22}	C_W^0	$\text{RMSD} \times 10^3$
0.437	9.58	0	0	805	0.0234	1.802
0.437	7.39	0	11.32	760	0.0234	1.035
0.437	10.55	-101	0	1073	0.0234	1.140
0.475	9.8	0	26.5	0	0.0234	2.655
0.437	1.4	225	33.9	0	0.0234	0.925
0.437	7.56	-1.5	10.7	780	0.0234	1.044

Note: All equilibrium constants are for the formation of the species from their respective monomers and are given in molar units.

TABLE XXVIII

COMPARISON OF THE LEAST SQUARES FITS FOR N-METHYL-
2-PYRROLIDONE AND N, N-DIMETHYLACETAMIDE
IN 1, 2-DICHLOROETHANE

NMP 25°C

K_{20}	K_{11}	K_{12}	K_{21}	K_{22}	C_W^0	$\text{RMSD} \times 10^3$
0	2.56	0	0	23.4	0.110	1.565
0	2.86	0	neg.	24.1	0.110	1.091
0	2.39	3.53	0	16	0.110	0.845
0	3.43	0	0.66	0	0.110	2.970
0	1.00	12.3	3.3	0	0.110	0.800
0	2.11	5.4	0.80	11.7	0.110	0.804

NMP 15°C

K_{20}	K_{11}	K_{12}	K_{21}	K_{22}	C_W^0	$\text{RMSD} \times 10^3$
0	4.02	0	0	28	0.080	1.842
0	3.80	0	5.4	16	0.080	1.492
0	3.82	5.73	0	16	0.080	1.491
0	4.80	0	0.008	0	0.080	3.001
0	3.05	12.0	2.2	0	0.080	1.306
0	2.7	16.5	3.5	-12.0	0.080	1.297

Note: All equilibrium constants are for the formation of the species from their respective monomers and are given in molar units.

TABLE XXVIII--Continued

NDMA 25^o C

K_{20}	K_{11}	K_{12}	K_{21}	K_{22}	C_W^o	$\text{RMSD} \times 10^3$
0	2.70	0	0	30.5	0.110	3.428
0	3.43	0	neg.	30.8	0.110	1.685
0	2.23	8.56	0	12.0	0.110	1.279
0	4.21	0	-0.89	0	0.110	3.985
0	1.1	15.7	2.6	0	0.110	1.197
0	2.35	7.8	-0.37	14.0	0.110	1.249

CHAPTER IV

DISCUSSION

The Self-Association of N-Methyl-2-Pyrrolidone

The predominant mechanism for the self-association of NMP in carbon tetrachloride and benzene is probably dipole-dipole association. Dipole association is particularly attractive since the dipole moment of NMP is approximately 4.06 D^{36} --a large dipole for a non-ionic molecule. Furthermore, the magnitude of the dimerization constants, K_{20} , of 0.71 and $0.39 \text{ (mole/liter)}^{-1}$ found for NMP in carbon tetrachloride and benzene, respectively, would seem to be in the proper range for dipolar associations. Treiner, Skinner and Fuoss,⁸⁴ for example, found a K_{20} of $0.37 \text{ (mole/liter)}^{-1}$ for p-nitroaniline and $0.8 \text{ (mole/liter)}^{-1}$ for m-nitrophenol in dioxane at 25°C , which have dipole moments of 4.38 and 6.91 D , respectively. Although the concentrations used in this study were low enough to render self-association of these compounds through hydrogen bonding undetectable, dioxane contains two strongly hydrogen bonding etheral oxygen atoms,⁸⁵ which would prevent it from acting as an inert solvent toward these solutes. Therefore, the dimerization constants for these compounds would be expected to be even larger in benzene

or carbon tetrachloride. A K_{20} of $0.71 \text{ (mole/liter)}^{-1}$ for NMP in carbon tetrachloride then seems to be quite reasonable.

Further justification of the magnitude of K_{20} in carbon tetrachloride can be inferred from the NMR work of Whittaker and Siegel⁶¹ as discussed in Chapter I. Briefly, the authors proposed dipolar association to explain the observed concentration dependence of $\Delta\delta_{\text{obs}}$, the separation of the N-methyl doublet of N-dimethylformamide, and since it had also been found that both the formyl proton and the mean N-methyl resonances were concentration independent. An association constant can therefore be calculated from the concentration- $\Delta\delta_{\text{obs}}$ relationships reproduced in Table XXIX. Since the upper limit of the concentration

TABLE XXIX

CONCENTRATION DEPENDENCE OF THE SEPARATION
OF THE N-METHYL DOUBLET OF N,N-DIMETHYL-
FORMAMIDE IN SEVERAL SOLVENTS 35°C

HMDS ^a		CCl ₄		Acetone -d ₆	
X _{DMF}	$\Delta\delta_{\text{obs}}^b$	X _{DMF}	$\Delta\delta_{\text{obs}}$	X _{DMF}	$\Delta\delta_{\text{obs}}$
0.0633	4.26 ± 0.13	0.110	8.19 ± 0.05	0.0858	8.94 ± 0.1
0.0480	3.98 ± 0.12	0.0666	7.76 ± 0.05	0.0169	8.90 ± 0.1
0.0362	3.54 ± 0.06	0.0444	7.48 ± 0.05	0.00845	8.87 ± 0.05
0.0244	3.26 ± 0.05	0.0222	7.08 ± 0.05	0.00634	8.81 ± 0.14
0.0182	3.08 ± 0.05	0.0111	6.57 ± 0.05	0.00426	8.85 ± 0.08
0.0122	2.91 ± 0.05	0.00833	6.47 ± 0.05	0.00169	8.83 ± 0.14
0.0037	2.66 ± 0.14	0.00557	6.34 ± 0.05		
		0.00222	6.16 ± 0.05		

^aHexamethyldisiloxane

^bc. p. s. at 54.6 Mc/sec

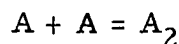
range studied by these workers was 10 mole percent, it is reasonable to assume only a monomer-dimer equilibrium to be involved, as was found for NMP. Then, expressing $\Delta\delta_{\text{obs}}$ as,

$$\Delta\delta_{\text{obs}} = \frac{C_M}{f_A} \Delta\delta_M + \frac{C_D}{f_A} \Delta\delta_D$$

where C_M and C_D are the molar concentrations of the monomeric and dimeric species with resonance separations of $\Delta\delta_M$ and $\Delta\delta_D$, respectively, and f_A the formal molar concentration of the amide. Since the highest polymerized state is taken to be dimeric,

$$f_A = C_M + 2K_{20}C_M^2$$

where K_{20} is the equilibrium constant for the reaction



Then,

$$\Delta\delta_{\text{obs}} = \frac{C_M \Delta\delta_M + 2K_{20}C_M^2 \Delta\delta_D}{C_M + 2K_{20}C_M^2}$$

Adding and subtracting $\Delta\delta_M$,

$$\text{obs} = \Delta\delta_M + \frac{C_M \Delta\delta_M + 2K_{20}C_M^2 \Delta\delta_D - C_M \Delta\delta_M - 2K_{20}C_M^2 \Delta\delta_M}{C_M + 2K_{20}C_M^2}$$

or,

$$\Delta\delta_{\text{obs}} = \Delta\delta_M + \frac{2K_{20}C_M^2}{f_A} (\Delta\delta_D - \Delta\delta_M) \quad (4-1)$$

As can be seen from equation (4-1), the correct value of K_{20} would

render a plot of $\Delta\delta_{\text{obs}}$ vs. $C_M^2 \div f_A$ linear, provided the dimer assumption is correct. Similarly, a value of K_{20} too small would give negative curvature and a K_{20} too large should give a positive curvature when plotted in this manner. In order to obtain the $C_M^2 \div f_A$ values for several trial dimerization constants, smoothed plots of $C_M^2 \div f_A$ vs. f_A were prepared for each K_{20} . From these plots $C_M^2 \div f_A$ values corresponding to the data given in Table XXIX, after conversion to a molar scale, could readily be obtained. The relationships found for carbon tetrachloride using dimerization constants of 0.5 and 1.0 (mole/liter)⁻¹ are illustrated in Figure XVIII where the circles and squares indicate the uncertainties reported by Whittaker and Siegel. The solid and dashed lines in this figure are arbitrarily drawn to indicate the general behavior. It can be seen that a K_{20} of 1.0 (mole/liter)⁻¹ comes very close to making the relationship between $\Delta\delta_{\text{obs}}$ and $C_M^2 \div f_A$ linear. However, the point for the highest concentration of N,N-dimethylformamide appears to fall significantly above the line. Therefore, a K_{20} of about 0.9 (mole/liter)⁻¹ might very well give a better fit of the data. Since N,N-dimethylformamide has a dipole moment of 3.86 D⁸⁶, which is only slightly lower than that for NMP, a dipole-dipole association constant of 0.9 (mole/liter)⁻¹ would seem to be in satisfactory agreement with a K_{20} of 0.71 (mole/liter)⁻¹ found for NMP in the same solvent. Interestingly, the data of acetone-d₆ also given in Table XXIX indicates that very little, if any, dipolar association occurs in this polar solvent.

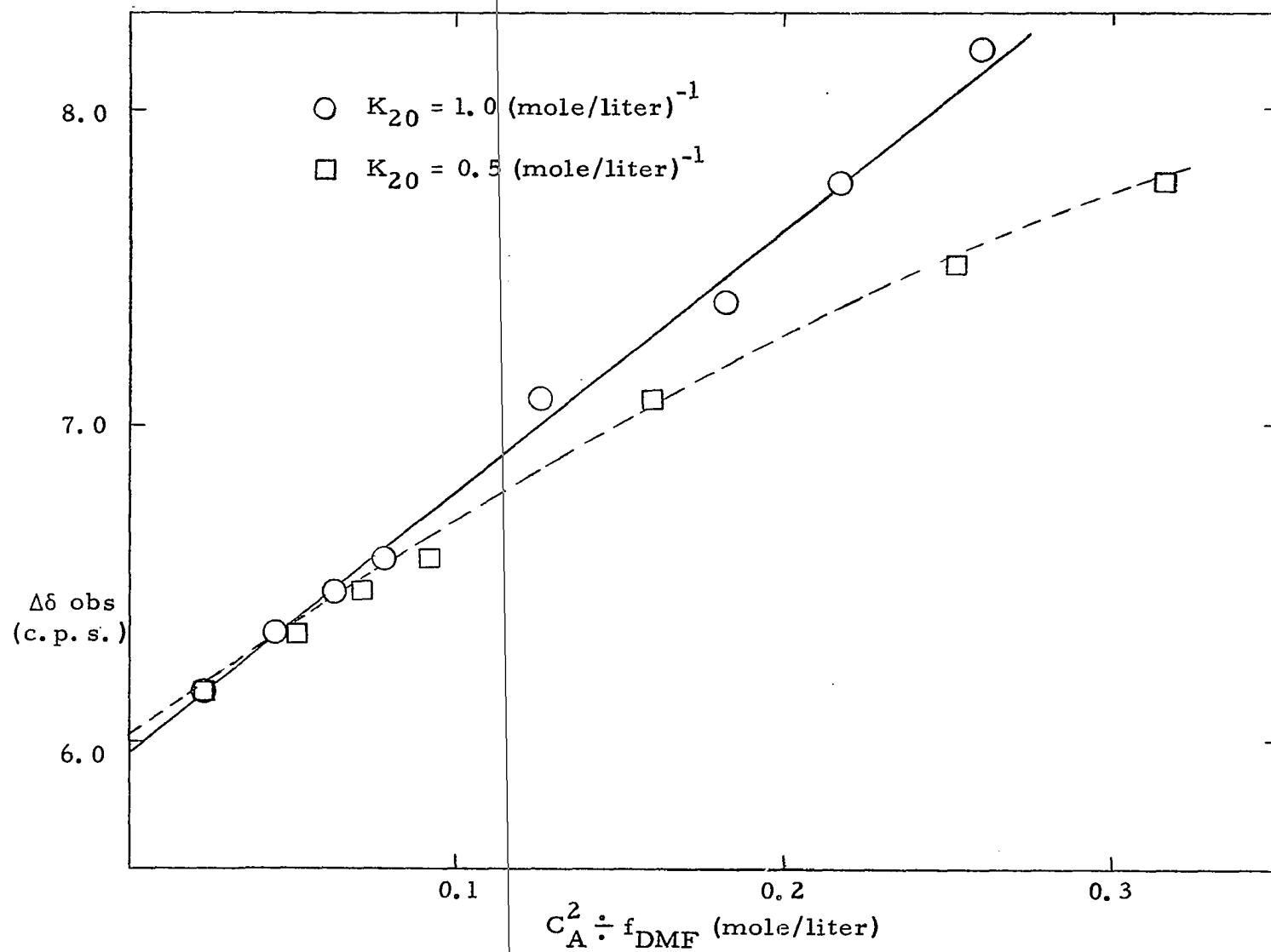


Figure XVIII. Graphical Estimation of K_{20} for N, N-Dimethylformamide in Carbon Tetrachloride 25°C

If only the polar properties of the solvent are considered, it would appear that K_{20} should be about the same order of magnitude in benzene as in carbon tetrachloride. However, Sandoval and Hanna,⁸⁷ using NMR techniques on cyclohexane solutions, have shown recently that benzene is involved in a specific interaction with N,N-dimethylformamide through what is apparently a charge transfer complex. An equilibrium constant of $0.128 \pm 0.0007 \text{ (mole/kg)}^{-1}$ at 37°C was obtained. Benzene, therefore, can not be considered an inert solvent for amides which perhaps accounts for the factor of about 2 between the dimerization constants in this solvent and carbon tetrachloride.

Although the dipole moment of NMP is sizeable, approximate calculations show that its dipolar association is not very energetic. As discussed in Chapter I the resultant dipole moment in a NMP molecule probably lies nearly coaxial with the C=O bond and coplanar with the amide group. Based on these assumptions, then, it appears that the saturated ring of NMP would prevent a head-to-tail arrangement of sufficient energy to account for the observed association. However, if it is assumed that the site of positive charge is near the carbonyl carbon atom and that the negative charge is located on the carbonyl oxygen, an antiparallel alignment of the dipoles appears to be feasible, where the carbonyl oxygen of one molecule lies directly above the carbonyl carbon of the other. From scale models, prepared using the C-N and C=O bond lengths of N-methylacetamide⁸⁷ and an average van der Waal's radius

for the hydrogens of the methylene and methyl group, antiparallel alignment of the resultant moments will allow an approach to within 4 Å.

Taking 4 Å as the distance of closest approach and assuming point dipoles, a maximum ΔU of about 1.9 kcal/mole is obtained from (4-2), the relation for antiparallel attraction,

$$\Delta U = \frac{\mu^2}{\epsilon a^3} \quad (4-2)$$

where a is the separation of the dipoles. Taking $\Delta U \approx \Delta H$, a value of 1.9 kcal/mole corresponds to an 11% increase in K_{20} for a 10°C drop in temperature. Consequently, a value of K_{20} 11% higher than the respective 25°C value was used for both solvents at 15°C.

The dimerization of NMP was neglected in the treatment of the hydration data in DCE since it can be shown from equation (4-2) using $\epsilon = 10.4$ at 25°C for DCE,⁸⁸ that $\frac{\Delta U}{\epsilon T} \approx 0.5$. Therefore, no extensive stabilization of the dipole pair would seem likely in this solvent. Furthermore, even if K_{20} were as much as 0.1 (mole/liter)⁻¹ in DCE the hydrate species and associations constants would not be significantly affected.

It is illuminating that acetone which has a dipole moment of only 2.80 D⁹⁰ has an antiparallel interaction energy of approximately 3.0 kcal/mole. This large energetic difference between the association of acetone and NMP reflects the importance of the distance of closest approach of the interacting dipoles. In addition, it is interesting that acetone, despite its greater energy of attraction, has a dimerization

constant of only $0.2 \text{ (mole/liter)}^{-1}$ in carbon tetrachloride,⁹¹ which is less than 1/3 that for NMP. This difference would seem to show the effect of the volume occupied by the associated pair. Treiner, et al.,⁸⁴ propose that the equilibrium constant for dipolar association is directly proportional to the volume of the pair. Based on scale models the anti-parallel dimer of NMP appears to have a volume of over $400 \text{ \AA}^3$ while that of acetone is between $100\text{-}200 \text{ \AA}^3$.

The Hydration of N-Methyl-2-Pyrrolidone and N, N-Dimethylacetamide

In Tables XXVI through XVIII, pages 121 through 124, the various least squares fits for all three solvents are compiled for ease of comparison. As stated in the last chapter none of the two-parameter fits were considered satisfactory since the RMSD for these were always 1.4 to 5 times higher than the best values. Closer examination of the fits for carbon tetrachloride and benzene show that only two of the three-parameter fits tried are satisfactory for all four systems. Furthermore, unrestricted four-parameter fits of the same data do not show a reduction in RMSD commensurate with the addition of a parameter as implied by equation (3-7). Thus, it appears that three parameters are sufficient to satisfactorily fit the hydration data.

In carbon tetrachloride at 25°C , where 33 data points were obtained from three activities, the lowest RMSD found was 0.995×10^{-3} mole/liter corresponding to the AW, A_2W and A_2W_2 fit. However, by

application of equation (3-7) the change in RMSD that is statistically significant for this system is 8 percent. Therefore, any fit with a RMSD of $(0.995 \times 10^{-3}) 0.08 = 0.08 \times 10^{-3}$ greater than 0.995×10^{-3} will be statistically inferior. A search of this portion of Table XXVI shows that only one additional set of species fall below the value of 1.075×10^{-3} mole/liter; that is, AW, A_2W , and AW_2 . For the 15°C data in carbon tetrachloride, with 44 points ($\Delta\text{RMSD} = \text{RMSD}(\text{min})0.07$), exactly the same situation obtains. The AW, A_2W and A_2W_2 set of species gave a RMSD of 0.659×10^{-3} mole/liter, and the set AW, A_2W and A_2W_2 gave 0.667×10^{-3} mole/liter, while all the remaining attempts may be considered statistically inferior.

The curve fitting results for the hydration of NMP in benzene at 25°C , where 58 samples were taken at four different activities, seem uniquely clear-cut. A RMSD of 0.852×10^{-3} mole/liter was found for the species AW, A_2W , and A_2W_2 , while the next best fit for any other set of species with all equilibrium constants positive was AW and A_2W_2 at 1.194×10^{-3} mole/liter; 40 percent higher. However, in the case of the 15°C data in benzene, for which 63 data points had been obtained, the AW, A_2W , and AW_2 choice yields a somewhat better fit at 0.925×10^{-3} mole/liter than the set AW, A_2W and A_2W_2 at a RMSD = 1.035×10^{-3} mole/liter.

In summary, for the four carbon tetrachloride and benzene systems, it appears that AW, A_2W and $A_2W_2^*$ adequately describe the

*In the future these two sets of species and their respective fits

functional relation between Δf_W and f_A in three of the systems while AW , A_2W , and AW_2^* also satisfy three of the systems but a different three. To choose between these two sets of species, the absolute and relative magnitudes of the individual constants and plausible geometries for the hydrated species must be considered.

A check of the magnitude of the constants associated with the AW_2 fit shows that K_{11} is always much smaller with this set than in the other fits. Indeed, $K_{11} = 1.4 \pm 0.8$ for benzene at 15°C and goes negative in the same solvent at 25°C . On this basis, then, the A_2W_2 set of species which gives a K_{11} of $6 \text{ (mole/liter)}^{-1}$ at 25°C in benzene would seem to be the more reasonable. Another important fact is that the unrestricted four-parameter fits in both solvent systems gave equilibrium constants nearly identical to those of the A_2W_2 fits.

Examination of the magnitude of K_{12} , compared to K_{11} , in the AW_2 fit provides further evidence against the AW_2 fit. Assume for the moment that the two sites in the cyclic amide, NMP, are equally basic. In the successive hydration reactions,



and



the forward rate constant, k_1 , of reaction (4-3) should be twice k_2 , the

will be referred to as the AW_2 or A_2W_2 fit since the other two species are common between them.

forward rate constant for reaction (4-4). In addition, k_{-2} , the rate constant for the dissociation of AW_2 should be $2k_{-1}$, since there are twice as many ways for AW_2 to dissociate, compared to AW . By combining the rate expressions it follows that

$$K_{12}^{SW} = \frac{k_2}{k_{-2}} = \frac{k_1}{4k_{-1}} = \frac{K_{11}}{4}$$

where K_{12}^{SW} is the step wise equilibrium constant for the formation of AW_2 .

But

$$K_{12}^{SW} = \frac{C_{AW_2}}{C_{AW}C_W} = \frac{C_{AW_2}}{K_{11}C_A C_W^2} = \frac{K_{12}}{K_{11}}$$

where K_{12} is the equilibrium constant for the formation of species AW_2 from its monomers, A and W.

Therefore,

$$K_{12} = \frac{K_{11}^2}{4}$$

In reality the basicities of the two sites in NMP are in all probability not equal, and K_{12} would be expected to be less than $\frac{K_{11}^2}{4}$.

From the AW_2 fit for NMP in carbon tetrachloride at 25°C a K_{11} of approximately $6 \text{ (mole/liter)}^{-1}$ was obtained. Based on the preceding argument a K_{12} of no more than $9 \text{ (mole/liter)}^{-2}$ would be anticipated. However, as can be seen from Table XXVI a monomer dihydrate constant of $316 \text{ (mole/liter)}^{-2}$ was calculated from the AW_2 fit. Similar large ratios of $\frac{K_{12}}{K_{11}^2}$ are found in the other three systems. Constants of

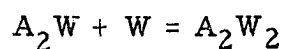
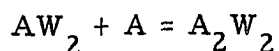
this magnitude would demand an enormous stabilization of the AW_2 species.

One form of stabilization is for the amide and the two water molecules to form a cyclic structure. However, if the hydrogen bond to the carbonyl oxygen is considered to be nearly linear and to be coplanar with the amide group, and if the formation of the hydrogen bond to the nitrogen is considered to occur nearly perpendicular to the plane of amide group, a highly stabilized (unstrained) cyclic structure can not be made from scale models. Furthermore, since the nitrogen lone pair is probably less basic than the oxygen lone pairs (see part III of the Introduction) the formation of a cyclic species involving both sites would not seem to be sufficiently energetic to stabilize such strained bond angles.

Another way that a monomer dihydrate species may be somewhat stabilized is that the second water molecule bonds only to the first. Frank and Wen,⁹² for example, argue that when a water molecule donates a proton to form a hydrogen bond, the water oxygen becomes more basic. The bonding of a second water molecule to this oxygen is then more energetic. However, the stabilization achieved in this way would not reasonably be expected to cause a 15-fold increase in K_{12} over K_{11} .

On the positive side, the apparent stability of the A_2W_2 species can be explained more readily. First there is a multiplicity of ways

that the A_2W_2 can be formed from bimolecular encounters,



where the presence of a small but perhaps undetectable concentration of AW_2 has been assumed. Second, on the basis of scale models and assuming the water molecules to bridge the two lactam molecules by hydrogen bonding to the carbonyl oxygen of one and the nitrogen of the other, a remarkable cyclic structure is achieved. This structure has at least four factors which contribute to its stability:

1) assuming an O-O and N-O hydrogen bond distance of 2.8 Å, the C=O groups of the two NMP molecules approach to within 3.5 Å; thereby a dipole-dipole interaction energy (antiparallel) contribution from the amide groups of approximately -5.5 kcal/mole is achieved;

2) the complex may be formed with all the normal bond angles preserved, thus the energy of hydrogen bonding is a maximum for the given interaction;

3) there would be an energy term derived from the dipole-dipole interaction of the amide group and its neighboring water molecule, ($\mu = 1.8$ D) which is probably slightly less than -3 kcal/mole;

4) there are four hydrogen bonds involved;

and finally, the group has a center of symmetry. Therefore, if an

average hydrogen bonding heat of formation of -3 kcal/mole is assumed, the formation of the species A_2W_2 should be accompanied by a $-\Delta H$ of approximately 20 kcal/mole, which seems more than adequate to explain its apparent stability. Therefore, despite the statistical equivalence of the two three-parameter fits under question, the A_2W_2 would appear to be the most reasonable on a structural and energetic basis.

The species A_2W which is common to both of the best fits of the hydration data for carbon tetrachloride and benzene is an interesting one as well. Mohr, Wilk and Barrow⁹² have studied the near infrared spectra of numerous Lewis bases, including acetone, dioxane and N, N-dimethylformamide, in water saturated carbon tetrachloride as a function of base concentration. For all the bases studied and generally around 0.2 mole/liter of base and 0.01 mole/liter of water the $\nu(OH)$ of H_2O splits into two bands. The higher frequency band was found to be narrow and only slightly shifted from the antisymmetric stretching mode, ν_3 , of free water in carbon tetrachloride at 3706 cm^{-1} . At higher base concentrations the sharp band disappeared and for the weaker bases it was replaced by two broad bands in the lower frequency region. In addition, the double band structure persisted to zero carbon tetrachloride concentrations. For the stronger bases at higher concentrations only a single broad band was apparent in the same region.

The disappearance of the ν_3 absorbance was taken as strong evidence that both hydrogens of a water were involved in hydrogen bonds.

Therefore, the predominant species present over the concentration range studied probably involves two base molecules and one water; that is a species corresponding to the A_2W found from the present study. Incidentally, the A_2W_2 species proposed above should have a near infrared spectrum nearly identical to that of A_2W .

Furthermore, the same workers found no detectable spectral changes as the formal concentration of water was raised to 0.2 mole/liter. However, at water concentrations above 0.2 mole/liter a broadening and intensification of the low frequency side of the absorption region became apparent. It was also noted that these changes were similar to those that occur in liquid water and give rise to the Raman shifts reported by Busing and Horning⁹³ at 3225 and 3450 cm^{-1} . These water to water absorbance bands might very well be due to molecular species such as AW_2 found in DCE from the work presented here.

Fortified with the spectral evidence for the A_2W species, the next consideration is its structure. In preparing a structure for the A_2W species the dipole moment of NMP should surely be considered since dipolar attraction plays a significant role in the stability of this molecular complex. From scale models it quickly becomes apparent that in any structure where the water molecule bridges the carbonyl group of the two lactam molecules, dipolar association between the NMP moments would be negligible due to their large separation and poor alignment. Furthermore, bridging between the nitrogens of the amide

groups would seem unlikely due to the apparent lower basicity of the amide nitrogen as compared to the oxygen and due again to the large separation and poor alignment of the dipoles. However, if one hydrogen bond is considered to occur coplanar with the amide group of the first NMP molecule and coaxial with the free-electron pair orbital of the carbonyl oxygen, and if the second hydrogen bond is taken nearly perpendicular to the nitrogen atom of the second NMP molecule, then the dipoles will be properly aligned and be sufficiently close to allow a significant interaction. In fact, if hydrogen bonding O-O and O-N distances of 2.8 Å are considered, the dipoles will approach to within 3.5 to 3.6 Å and a dipolar heat of formation of -4 or 5 kcal/mole will be realized. This effect, combined with the formation of two hydrogen bonds would seem to account for the observed stability of the A_2W species. Thus, the predominant structure for the A_2W species is probably the anhydrous dipolar dimer 'glued' together with a water molecule. In addition, the proposed A_2W structure is the same as that for the A_2W_2 species with one water molecule removed.

The order of magnitude expected for the formation constant associated with the A_2W species is also of interest. If A_2W is considered to be formed from the following equilibria,



and if there is no a priori difference in the hydrogen bonding ability of the second hydrogen of water once the first has bonded, k_2 should equal $\frac{1}{2} k_1$, since there are only half the number of sites available to the second A molecule. Similarly, k_{-2} should equal $2k_{-1}$, since there are two ways that A_2W can dissociate and only one for AW . Therefore, following an argument completely analogous to that applied to AW_2 , it can be seen that,

$$K_{21} = \frac{K_{11}^2}{4}$$

For NMP in carbon tetrachloride at 25°C K_{11} was found to be 9.2 (mole/liter)⁻¹. Therefore, if the above reasoning is correct, K_{21} should equal 21 (mole/liter)⁻² at this temperature. As can be seen from Table XXVI, K_{21} of 39 (mole/liter)⁻² was actually found. This enhancement of K_{21} over $K_{11}^2/4$ probably indicates that A_2W can be formed in more ways than assumed in equilibria (4-5) and (4-6). For benzene, however, K_{21} is only about half of $K_{11}^2/4$, which indicates that the solvent effects are more important toward higher species.

Turning to the hydration studies in DCE, it can be seen from Table XXVIII that the best least squares fits for the three sets of data are AW , A_2W , AW_2 and AW , AW_2 , A_2W_2 . For NMP in DCE at 25°C, where 58 pieces of data were collected, the A_2W fit gave an RMSD of 0.800×10^{-3} mole/liter and A_2W_2 had a RMSD = 0.845×10^{-3} mole/liter. Once again, application of equation (3-7) indicates that these two fits are statistically equivalent. Similar to the situation with benzene at

15°C, however, the AW_2 fit for NMP in DCE at 15°C with $n = 63$ appears to give a statistically superior fit. Thus, we are again faced with the problem of two essentially equivalent statistical treatments for NMP in DCE.

Based on the 7 to 9-fold decrease of K_{21} in passing from carbon tetrachloride to benzene, it is unreasonable that K_{21} should be as large as $3.3 \text{ (mole/liter)}^{-2}$, particularly since it was only 4.2 in benzene. Furthermore, in the A_2W fit of the hydration data at 25°C, K_{21} was negative and in the two-parameter AW and A_2W fit, K_{21} was negligible as it was for the 15°C data. Exactly, the same situation was observed for K_{21} , with the hydration data of N,N-dimethylacetamide (NDMA) in DCE, which would not be expected to act significantly differently toward hydration. In addition, with the AW_2 fit K_{11} decreases by an unreasonable factor of 3 for a 10°C temperature interval. Therefore, the only set of species which consistently satisfied all three sets of data and gave reasonable values of the higher hydration constants is AW , AW_2 , and A_2W_2 .

The fact that the species AW_2 has become important in DCE while it apparently wasn't in carbon tetrachloride and benzene is no doubt due to the mass action effect resulting from the much greater water solubility in this solvent. Even a K_{12} five times as great as the $3.5 \text{ (mole/liter)}^{-2}$ found for NMP in DCE at 25°C would give a species concentration of only 0.0026 mole/liter in benzene at the highest water

$$f_A = C_A + K_{11}C_A C_W + 2K_{20}C_A^2 + 2K_{21}C_A^2 C_W + 2K_{22}C_A^2 C_W^2$$

TABLE XXX--Continued

$$= C_A + 6.0C_A C_W + 2(0.39)C_A^2 + 2(4.3)C_A^2 C_W^2 + 2(430)C_A^2 C_W^2$$

$$\text{and } \Delta f_W = 6.0C_A C_W + 4.3C_A^2 C_W + 2(430)C_A^2 C_W^2$$

C_A	C_W	C_{AW}	C_{A_2W}	$C_{A_2W_2}$	C_A	Δf_W	f_A
0.1	0.01	0.0060	0.0004	0.0004	0.0039	0.0072	0.1154
0.1	0.02	0.0120	0.0008	0.0016	0.0039	0.0160	0.1246
0.3	0.01	0.0180	0.0039	0.0039	0.0351	0.0297	0.3987
0.3	0.02	0.0360	0.0078	0.0156	0.0351	0.0740	0.4730

The lactam monomer concentration, C_A , and monomer water concentration, C_W , used to make up this table approximate the experimental concentration range of Δf_W and f_A . It is immediately apparent in carbon tetrachloride that as the concentration of NMP is raised the importance of species A_2W rises rapidly until at a monomer concentration of 0.3 molar it becomes the major hydrated species. It is also noteworthy that the species concentration of A_2W_2 is quite small over the experimental range, despite its large equilibrium constant, as was indicated in the plot of Δf_W vs. $(f_A - \Delta f_W) a_W$ (Figure X).

Turning to the benzene data, quite a different situation is seen.

The concentration of A_2W is now the least important over the experimental range studied and A_2W_2 has become relatively much more

important. However, the monomer monohydrate still makes up the bulk of the hydrate concentration in this solvent. The rising importance of the species A_2W_2 is apparently due to the mass action effect resulting from the approximate 4-fold increase in the solubility of water in benzene over that in carbon tetrachloride, since K_{22} in benzene is only 1/3 of that in carbon tetrachloride.

Hydrate species concentrations for NMP in DCE at 25°C are given in Table XXXI. Noteworthy is the fact that the monomer monohydrate

TABLE XXXI

HYDRATE SPECIES CONCENTRATIONS OF N-METHYL-2-PYRROLIDONE IN 1, 2-DICHLOROETHANE 25°C

$$f_A = C_A + K_{11}C_A C_W + K_{12}C_A C_W^2 + 2K_{22}C_A^2 C_W^2$$

$$= C_A + 2.4C_A C_W + 3.5C_A C_W^2 + 2(16)C_A^2 C_W^2$$

$$\text{and } \Delta f_W = 2.4C_A C_W + 2(3.5)C_A C_W^2 + 2(16)C_A^2 C_W^2$$

C_A	C_W	C_{AW}	C_{AW_2}	$C_{A_2W_2}$	Δf_W	f_A
0.1	0.02	0.0048	0.0001	0.0003	0.0056	0.1055
0.1	0.08	0.0192	0.0011	0.0051	0.0316	0.1305
0.4	0.02	0.0192	0.0003	0.0010	0.0218	0.4215
0.4	0.08	0.0768	0.0045	0.0154	0.1066	0.5121

species, AW , has become the largest species by at least a factor of

five at the highest experimental concentrations of lactam and water.

Once again it can be seen that solvent polarity has a more pronounced effect on the highly polymerized species. Although A_2W_2 is the second largest species, it makes a contribution of only 15% toward the total hydrate species concentration. The species AW_2 contributes less than 5% to the total, but is still apparently a significant species.

Further justification for the equilibrium constants reported here can be offered by comparison with the literature values. As stated in Chapter I, to the author's knowledge only three quantitative studies other than this one have been conducted on the hydration of amides in organic solvents. The first of these was the near infrared work of Worley² with 2-pyrrolidone and NMP in carbon tetrachloride at 25°C. By following both the free $\nu(OH)$ band at 2.680μ and the hydrate absorbance at 2.860μ as a function of NMP concentration and water activity. Worley reported a K_{11} of $16.2 \text{ (mole/kg)}^{-1}$ which corresponds to a K_{11} of about $11 \text{ (mole/liter)}^{-1}$. Comparison of the monomer monohydrate constant for NMP in carbon tetrachloride at 25°C given in Table XXVI shows that the spectral constant is nearly 1.2 times as large. Although the self-association of NMP would be negligible over the concentration range that Worley used (up to 0.04 mole/liter), the contribution of A_2W at these concentrations appears to be significant. Using $K_{21} = 39 \text{ (mole/liter)}^{-2}$, $K_{11} = 9.2 \text{ (mole/liter)}^{-1}$ and $C_A = 0.03 \text{ mole/liter}$, the concentration of species A_2W would be about 0.003 and that for AW would be

only 0.0024 mole/liter. Therefore, at a formal lactam concentration less than the maximum used in the spectral study the A_2W would represent over 10% of the total hydrate concentration. The presence of additional species then might account for most of the difference in the two K_{11} values.

The second study of the hydration of the amide group in non-hydroxylic solvents was the vapor pressure and solute isopiestic experiments of Grigsby.³ Working with carbon tetrachloride solutions of N-methacetamide at 25°C Grigsby found a monomer monohydrate equilibrium constant of 12 (mole/liter)⁻¹. This value is only slightly higher than the K_{11} of 9.2 mole/liter reported here. Furthermore, a slightly higher value of K_{11} might be anticipated for this compound since any contribution from $N-H \cdots O \begin{smallmatrix} H \\ \diagup \\ H \end{smallmatrix}$ bonding would be reflected in the observed 1:1 equilibrium constant.

The recent NMR work of Takahashi and Li¹⁷ constitutes the third quantitative study of the interaction of amides with water. These workers concluded from a study of N,N-dimethylformamide and water in cyclohexane solutions that one of the major species present was A_2W ; that is a water bridging two amide molecules. However, to obtain a water proton spectrum with this system it was necessary to use amide concentrations in excess of 0.5 mole fraction. Therefore, the constants can not be considered those for an inert solvent. Furthermore, an equilibrium constant for the formation of the 1:1 species could not be

calculated from the NMR data. Consequently, the 2:1 constant of $0.24 \text{ (mole/liter)}^{-1}$ at 35°C obtained was for the step-wise reaction and a direct comparison to the 2:1 constant presented here, which was calculated from monomers, can not be made. However, from the data in Table XXVI a step-wise constant ($K_{21}^{\text{SW}} = K_{21}/K_{11}$) of approximately 4 for carbon tetrachloride at 25°C is found. This 16-fold difference in step-wise constants for the 2:1 species probably results from the high polarity of the solvent used in the NMR study, since a slightly larger constant would be expected for the same association in dilute cyclohexane over that in carbon tetrachloride.

CHAPTER v

CONCLUSIONS

Self-Association of N-Methyl-2-Pyrrolidone

It has been shown that vapor pressure lowering affords a convenient and precise method for the evaluation of dipolar association constants. The standard deviations found for K_{20} of less than 10% strongly reflect the size of the association constant. For a constant much greater than 3 and certainly for constants larger than 10 (mole/liter)⁻¹ vapor pressure lowering would be much less precise. However, dipolar association of most molecular compounds would probably fall into the range 0 to 3 (mole/liter)⁻¹. Therefore, vapor pressure lowering is surely one of the best methods available to obtain dipolar association constants of non-volatile polar solutes in volatile solvents over a concentration range of 0.1 to 0.5 mole/liter. In addition, by way of general information, it may be concluded that in complex equilibria studies above 0.1 mole/liter with fairly polar compounds ($\mu > 2D$) in non-polar solvents, dipolar association must be taken into account.

Hydration of N-Methyl-2-Pyrrolidone

It has been shown that NMP is extensively hydrated in nonhydroxylic solvents. Therefore in any distribution of amides or lactams between water and some immiscible organic solvent, such as the study conducted by M. Davies and H. E. Hallem,⁹⁵ the hydration of the amide in the organic phase can not be neglected. Interestingly, it has also been seen that the percentage of hydration of NMP increased in the order carbon tetrachloride < benzene < 1,2-dichloroethane while the hydration constants decreased in the order carbon tetrachloride > benzene > 1,2-dichloroethane. Thus, it appears that the mass action effect resulting from the increased water solubility is more important than solvation effects.

Table XXXII summarizes the self-association and hydration data for N-methyl-2-pyrrolidone and N,N-dimethylacetamide in the three solvents studied. The monomer monohydrate, K_{11} , formation constants are of particular interest since there are two sites available for hydration in an amide group. Gregory⁹⁶ has found monomer monohydrate constants of 2.5 and 3.5 (mole/liter)⁻¹ in benzene at 25°C for triethylamine and N,N-dimethylcyclohexylamine, respectively. On the other hand, a 1:1 equilibrium constant of 6.0 (mole/liter)⁻¹ was found for NMP in benzene at 25°C. Therefore, it may reasonably be concluded from these data that the amide nitrogen is not the only site hydrating in NMP. Furthermore, based on the discussion in the last two sections of Chapter I, an amide nitrogen should have a reduced basicity as compared to an

TABLE XXXII

SUMMARY OF THE HYDRATION AND SELF-ASSOCIATION OF N-METHYL
2-PYRROLIDONE AND N,N-DIMETHYLACETAMIDE

	N-Methyl-2-Pyrrolidone						N, N-Dimethylacetamide
Solvent	Carbon Tetrachloride		Benzene		1, 2-Dichloroethane		1, 2-Dichloroethane
Temp ^o C	15	25	15	25	15	25	25
K ₂₀	0.79	0.71 $\pm$.06	0.44	0.39 $\pm$.04	0	0	0
K ₁₁	8.3 $\pm$ 0.8	9.2 $\pm$ 1.0	7.4 $\pm$ 0.2	6.0 $\pm$ 0.1	3.82 $\pm$ 0.08	2.39 $\pm$ 0.06	2.23 $\pm$ 0.07
K ₁₂	0	0	0	0	5.7 $\pm$ 0.6	3.5 $\pm$ 0.4	8.6 $\pm$ 0.9
K ₂₁	73 $\pm$ 3	39 $\pm$ 4	11.3 $\pm$ 1.0	4.3 $\pm$ 0.6	0	0	0
K ₂₂	2400 $\pm$ 500	1330 $\pm$ 180	760 $\pm$ 32	430 $\pm$ 15	16 $\pm$ 2	16 $\pm$ 2	12 $\pm$ 2

All constants are for the formation of the species from their respective monomers and are given in molar units.

amine. Consequently, if the basicity of the amide nitrogen in NMP is reduced, by, say, one-half from that of an average tertiary amine, then a K_{11} of 6.0 would mean that there is a 4:1 or 5:1 statistical preference for hydration at the carbonyl oxygen.

Another interesting feature of the data summarized in Table XXXII, is the effect of solvent on the hydration constants. For example, K_{11} decreases by a factor of approximately 5 in passing from carbon tetrachloride to 1,2-dichloroethane. The more highly polymerized species, however, show a much more pronounced effect and indeed K_{22} decreases by 80-fold over the same solvent range. Large reductions such as this would seem to offer strong evidence that the more complex species are less favorably solvated than the monomers. Therefore, the formation of higher species "costs" more energy in highly polar solvents. The fact that the higher species are less solvated would seem reasonable if most of the solvation effects in these solvents were of a dipolar nature. Greater solvation of the lower species would then be due to the more polar nature of these species.

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